

لو مريض كان ال srcr عنده = 0.8 mg/dl
وبدا ب دوا معين X وبعد أسبوع قيسنا ال SrCr وكان 2mg/dl

او مريض تعرض لنزيف ووصل ال srcr عنده ل 1.9 mg/dl

□ Srcr = serum creatinine □
□ □ Normal srcr 0.5 -1.2 mg/dl
شو تفسيرنا للقراءات ؟□□□

من المعروف انه ال Kideny بالوضع الطبيعي بيوصلها 25% من ال Cardiac output وبتملله فلترة ب rate بنسميه ال GFR
والفلتره رح تخلص الجسم من ال Waste product زي ال Creatinine وال Urea ..
وارتفاع نسبه ال Creatinine بالدم معناته انه ال GFR قل ومش قادره تفلتر الكميه المطلوبه وتخلص من ال Waste Product

□□ Normal GFR 90-120ml/min

يعني كل دقيقه الكليه رح تفلتر 90-120 مل من الدم

نرجع للمثاليين اللي ضربناهم المريضين كان عندهم Normal srcr وبعد فتره قصيره ارتفعت قيم ال SrCr عن الطبيعي
معناته المريض دخل ب □ (Acute Kideny Injury) (AKI)

تعالو نبليش بموضوع ال Acute kideny Injury ونشوف تفاصيله

اول شي نشوف تعريف ال AKI

□ Acute kidney injury (AKI) :
is an abrupt and usually reversible decline in the glomerular filtration rate (GFR). This results in elevation of serum blood urea nitrogen (BUN), creatinine, and other metabolic waste products that □are normally excreted by the kidney

يعني صار خلل ما أدى ل قله ال GFR وبالتالي تراكمت ال Waste product بالجسم
ال AKI يعتبر Reversible يعني once صلحنا السبب بترجع ال kideny لشغلها الطبيعي ...□□
ومدته ممكن تكون ساعات او ايام او اسابيع
ع الاغلب لحد 3 شهور بنسميه AKI
لو كان ال srcr مرتفع لاكثر من 3 شهور معناتها ع الاغلب المريض
(Chronic kideny diseases (CKD

□ طيب كيف اتأكد من انه المريض دخل ب AKI □□
في عنا منظمه ال KDIGO حكيت عشان احلف انه المريض AKI

VISIT...

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لازم يكون عنده

one or more of three criteria

علامه وحده ع الاقل من العلامات التاليه :

1□a rise in serum creatinine of at least 0.3 mg/dL
(26.5 micromol/L) over a 48-hour period

يعني شخص كان ال srcr عنده 1.1 صار 1.4

Srcr rise ≥ 1.5 times the baseline value within the seven previous days 2□

□ وحسب منظمه ال AKIN

Srcr rise ≥ 1.5 times the baseline value within 48 hour

يعني ارتفاع بال srcr مره ونص ،، فلو كان 1 يصير 1.5

3□urine volume ≤ 0.5 mL/kg per hour for six hours

□ لو المريض عنده علامه من هاي العلامات معناته AKI

في عنا منظمات صنفه مرضى ال AKI ل Stages حسب قديش قيمه ال srcr وال Urine output
وكل ما كان المريض بال Stages الاولى كل ما كان أفضل

واشهر ثلاث تصنيفات هي :

1□RIFLE criteria

R: Risk of renal dysfunction

I : Injury Of kidney

F: Fauiler of Kidney function

L:Loss of kidney function

E: End stage kidney disease

2□AKIN criteria: (Acute Kidney Injury Network)

(3□KIDGO critiria (Kidney Disease: Improving Global Outcomes

نشوف ال Staging حسب ال KIDGO

□Stage 1 : Increase in serum creatinine of ≥ 0.3 mg/dL

OR

1.5 to 1.9 times baseline

OR

Urine output of <0.5 mL/kg/hour for 6 to 12 hours

□Stage 2 : Increase in serum creatinine to 2.0 to 2.9 times baseline

OR

Urine output of <0.5 mL/kg/hour for 12 to 24 hours

□Stage 3: Increase in serum creatinine to ≥ 3.0 times baseline

OR
Increase in serum creatinine of ≥ 0.3 mg/dL to ≥ 4.0 mg/dL¶

OR
Urine output of < 0.3 mL/kg/hour for ≥ 24 hours or anuria for ≥ 12 hours

OR
(Initiation of renal replacement therapy (as Dialysis

بالنسبة لل AKIN وال RIFLE شبه مطابقين لل KIDGO ورح نرفقهم بجدول

هيك بنكون عرفنا تعريف ال AKI وشو ال Diagnostic criteria اللي يعتمد عليها لاحكي انه فعلا المريض دخل ب AKI
وشو ال Stages الي المريض بيكون فيها حسب ال Srcr وال Urineoutput

آخر شي لازم نعرفه انه مريض ال AKI ممكن يكون Oligurea
او Anuria او Non oligurea

Oligurea: urineoutput 50-500 ml /24 hr
Anuria : urine output less than 50 ml /24 hr
Nonoligurea : urine output more than 500 ml/ 24 hr

البوست القادم ان شاء الله رح نشوف الاسباب اللي بتدخل المريض ب AKI
Prerenal Causes ,,Internsic Causes ,,Post Renal Causes

#لعلي_أفيدك ٩٩



Serum Creatinine Criteria				Urine Output Criteria
	RIFLE	AKIN	KDIGO	
1—R	$>1.5 \times$ baseline or GFR decrease $>25\%$	≥ 0.3 mg/dL increase or $\geq 1.5\text{--}2 \times$ baseline	$1.5\text{--}1.9 \times$ baseline or >0.3 mg/dL increase (within 48 h)	<0.5 mL/kg/h for 6–12 h
2—I	$>2 \times$ baseline or GFR decrease $>50\%$	$>2\text{--}3 \times$ baseline	$2\text{--}2.9 \times$ baseline	<0.5 mL/kg/h for 12 h
3—F	$>3 \times$ baseline or Cr >4 mg/dL with an acute rise >0.5 mg/dL	$>3 \times$ baseline or ≥ 4.0 mg/dL with acute increase of ≥ 0.5 mg/dL or initiation of RRT	$3 \times$ baseline or increase in serum Cr ≥ 4 mg/dL or initiation of RRT	<0.3 mL/kg/h for 24 h or anuria for 12 h
L	Loss of renal function >4 wk			$\leftarrow$ Outcome classes for RIFLE criteria
E	End-stage renal disease			

GFR criteria

Urine output criteria

Risk

Increased creatinine $\times 1.5$ or
GFR decrease $> 25\%$

UO $< 0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$
 $\times 6 \text{ h}$

High sensitivity

Injury

Increased creatinine $\times 2$ or
GFR decrease $> 50\%$

UO $< 0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$
 $\times 12 \text{ h}$

Failure

Increased creatinine $\times 3$ or
GFR decrease $> 75\%$ or
creatinine $\geq 4 \text{ mg per}$
100 ml (acute rise of
 $\geq 0.5 \text{ mg per 100 ml dl}$)

UO $< 0.3 \text{ ml kg}^{-1} \text{ h}^{-1}$
 $\times 24 \text{ h}$ or
anuria $\times 12 \text{ h}$

Oliguria

High specificity

Loss

Persistent ARF = complete loss of
renal function $> 4 \text{ weeks}$

ESRD

End-stage renal disease

Criteria for acute kidney injury

	RIFLE ^[1]	AKIN ^[2]	KDIGO ^[3]
Diagnostic criteria*			
		Increase in serum creatinine of ≥ 0.3 mg/dL or $\geq 50\%$ within 48 hours OR Urine output of < 0.5 mL/kg/hour for > 6 hours	Increase in serum creatinine of ≥ 0.3 mg/dL within 48 hours or $\geq 50\%$ within 7 days OR Urine output of < 0.5 mL/kg/hour for > 6 hours
Staging criteria			
Risk (RIFLE) or stage 1 (AKIN/KDIGO)	Increase in serum creatinine to 1.5 times baseline OR Urine output of < 0.5 mL/kg/hour for 6 to 12 hours	Increase in serum creatinine of ≥ 0.3 mg/dL or to 150 to 200% baseline OR Urine output of < 0.5 mL/kg/hour for 6 to 12 hours	Increase in serum creatinine of ≥ 0.3 mg/dL or 1.5 to 1.9 times baseline OR Urine output of < 0.5 mL/kg/hour for 6 to 12 hours



Graphic



Injury (RIFLE)
or stage 2
(AKIN/KDIGO)

Increase in
serum
creatinine of
to 2 times
baseline

OR

Urine output
of <0.5
mL/kg/hour
for 12 to 24
hours

Increase in
serum
creatinine to
200 to 300%
baseline

OR

Urine output
of <0.5
mL/kg/hour
for 12 to 24
hours

Increase in
serum
creatinine to
2.0 to 2.9
times
baseline

OR

Urine output
of <0.5
mL/kg/hour
for 12 to 24
hours



Graphic



Failure
(RIFLE) or
stage 3
(AKIN/KDIGO)

Increase in
serum
creatinine to
3 times
baseline

OR

Increase in
serum
creatinine
by >0.5
mg/dL to
 >4.0 mg/dL

OR

Urine output
of <0.3
mL/kg/hour
for >24
hours or
anuria for
 >12 hours

OR

Initiation of
renal
replacement
therapy

Increase in
serum
creatinine to
 $>300\%$
baseline

OR

Increase in
serum
creatinine
by >0.5
mg/dL to
 ≥ 4.0 mg/dL

OR

Urine output
of <0.3
mL/kg/hour
for >24
hours or
anuria for
 >12 hours

OR

Initiation of
renal
replacement
therapy

Increase in
serum
creatinine to
 ≥ 3.0 times
baseline

OR

Increase in
serum
creatinine of
 ≥ 0.3 mg/dL
to ≥ 4.0
mg/dL[¶]

OR

Urine output
of <0.3
mL/kg/hour
for ≥ 24
hours or
anuria for
 ≥ 12 hours

OR

Initiation of
renal
replacement
therapy

Loss (RIFLE)	Need for renal replacement therapy for >4 weeks		
End stage (RIFLE)	Need for renal replacement therapy for >3 months		

RIFLE: risk, injury, failure, loss, ESRD; AKIN: Acute Kidney Injury Network; KDIGO: Kidney Disease: Improving Global Outcomes; ESRD: end-stage renal disease.

* AKIN and KDIGO provided both diagnostic and staging criteria. RIFLE provided a graded definition of AKI that is implicit in the staging criteria.

¶ In patients <18 years, stage 3 AKI is also defined by KDIGO as a decrease in estimated glomerular filtration rate (eGFR) to <35 mL/min/1.73 m².

تكلما البوست السابق عن تعريف ال AKI
وال staging تبعه حسب ال KDIGO وال AKIN وال RIFLE ..

اليوم ان شاء الله رح ندخل بالمهم ونشوف شو الاسباب اللي بتدخل المريض ب AKI ...

في عنا تقسيمه مشهوره لل AKI causes حسب شو اللي تأثر بالكلية كالتالي ::
Pre Renal AKI -1

هنا خلايا الكلية سليمة وما صار فيها خلل انما في سبب قلل كمية الدم الواصل للكلية
يعني الخلل مش بالكلية نفسها ، انما بال Blood amount اللي واصل للكلية
لما تقل كمية الدم الواصله للكلية ، تلقائي بيقل ال GFR وبتتراكم
ال waste product في الجسم

GFR is diminished because of decreased renal blood flow
وكمان شوي رح نفصل ال Pre Renal Causes

(2-Interinsic (Renal) AKI (ACute Tubular Necrosis ATN

هنا الكلية صار فيها Damage و صار في necrosis لخلايا الكلية
وغالبا السبب Toxins او المريض كان عنده Pre Renal AKI وما تعالج ف ال Ischemia أثرت ع خلايا الكلية و صار فيها
Necrosis

3-Post Renal AKI :

هنا سبب ال AKI انه في Obstruction عامل انسداد لمسار ال urine
فما يقدر يعدي ال Urine وبالتالي ال Waste product رح ترجع وتتراكم بالدم

نشوف اول نوع وهو ال Pre Renal AKI :

لو رجعنا لستركشر النيفرون
Nephron is consist of Glomerulus and Tubule

ال Glomerulus داخل فيها Afferent aretry جايب الدم من ال Renal aretry وبيدخله لداخل (المصفاه Glomerulus)
بعد ال Afferent في شبكه من ال capillary اللي بتختار مكونات الدم اللي رح تعدي من ال Glomerulus ويدخل لل Tubule
زي ال Electrolyte وال urea وال creat بتتصفى وبتدخل لل Tubule
وبالمقابل ال plasma protein زي ال Albumin بترجع للدم وما بتعدي ال Tubule

وبعد شبكه ال Capillary بيطلع من ال Glomerulus ال Efferent aretry اللي بيكون ضيق مقارنه بال Afferent

طيب شو الحكمه انو يكون ال Afferent aretry والاسع ،، وال Efferent ضيق ؟

ال Afferent واسع ويدخل كميته الدم المطلوبه للفلتره ..
ولازم الدم يقعد فترة داخل ال Glomerulus عشان يصير اختيار لمكونات الدم اللي رح تعدي لل Tubule

وال Efferent يكون ضيق عشان لما يدخل الدم من ال Afferent ما يطلع بسرعه بال Efferent
ويضل لغيره ويرفع ضغط ال Glomerular capillary ويسمح بعملية الفلتره

عشان هيك لازم ال Efferent يكون ضيق عشان تصير عمليه الفلتره

إذا بنتوقع لو صار Vasoconstriction لل Afferent aretry
رح تقل كميته الدم الواصل لل Glomerulus وبالتالي يقل ال GFR

ولو صار Vasodilatation لل Efferent , الدم رح يطلع بسرعه من ال glomerulus وبالتالي يقل ال Glomerulus
capillary pressure □ وبتقل عمليه الفلتره وبالتالي يقل ال GFR

طبيب شو هي الاسباب اللي بتدخل المريض ب : Pre Renal AKI

□●When renal ischemia is part of a generalized decrease in tissue perfusion

يعني صار decrease في Tissue perfusion لكل انحاء الجسم ومن ضمنهم الكليه : ومن الامثلة اللي بتوصل الجسم ل
Hypoperfusion

□●True volume depletion ➡ decrease blood volume ➡ decrease in GFR

Volume depletion may be caused by gastrointestinal disease (vomiting, diarrhea, bleeding), renal losses (diuretics, glucose osmotic diuresis), skin or respiratory losses (insensible losses, sweat, burns), and third space sequestration (crush injury or skeletal fracture).

□●Hypotension - Severely decreased blood pressure can result from shock (hypovolemic, myocardial, or septic) and posttreatment of severe hypertension.

Decrease blood pressure ↓, Decrease GFR ↓

□●Edematous states - Heart failure and cirrhosis can result in marked reductions in kidney perfusion

Decrease Cardiac output ↓, decrease tissue perfusion

□●When there is selective renal ischemia

□●Selective renal ischemia - Bilateral renal artery stenosis or unilateral stenosis in a solitary functioning kidney

يعني لو كان في stenosis ضيق بال Renal Aretry المغذي لل
Right and left kidney

او مريض عنده كليه واحده بس ،فرضا Right kidney و صار Stenosis لل renal aretry المغذي للكليه....

● Drugs affecting glomerular hemodynamics

Drugs that affect glomerular hemodynamics can reduce the glomerular filtration rate (GFR) by lowering the intraglomerular pressure that drives this process

مبين الأدوية التي بتأثر ع ال : GFR

1: NSAIDs

ال NSAIDs الميكانيزم لالها انها بتمنع تكوين ال COX enzyme

وبالتالي بتمنع تكوين ال (Prostaglandin (PG

ال PG وخصوصا ال PGE2 وال (PGI2) وظيفتهم : increase renal blood flow by vasodilatation effect and glomerular filtration rate

فلما ال NSAIDs تمنع تصنيع ال PG رح يصير vasoconstriction لل Renal Artery وبالتالي بيقل ال GFR

2: ACEIs or ARBs

ال (Angiotensin 2 (Ang 2 يعمل Vasoconstriction لل Efferent

وبالتالي يحافظ ع ال Capillary pressure والفلتره

فأدويه ال ACEIs وال ARBs بتمنع تكوين ال Ang 2 , وبالتالي بينفك ال V.C التي على ال Efferent ويبقى ال capillary pressure

3: calcineurin inhibitors

زي ميكانيزم ال NSAIDs

إذا الخلاصة لل Pre Renal AKI انه الدم الواصل للكلية (لأي سبب من الأسباب التي قلناها) قل وبالتالي قل ال GFR وتراكمت ال Waste product بالجسم

البوست القادم ان شاء الله رح نشوف التحاليل التي بنعرف منها انه سبب ال AKI هي Pre Renal وكيف بنقدر نعمل

Prevention لل prerenal AKI وكيف علاج ال Pre Renal AKI

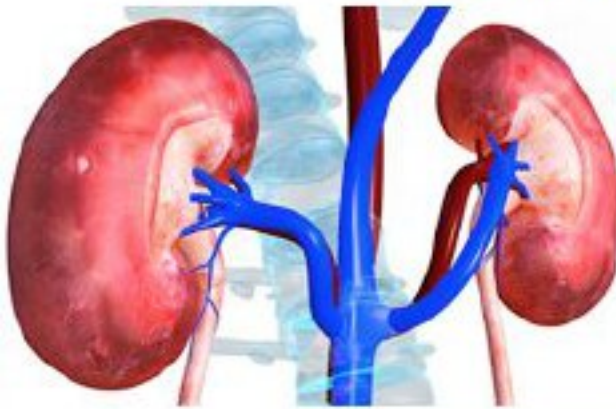
#لعلي_أفيدك ٩

Acute Kidney Injury

Prerenal

Inadequate perfusion

- Leads to decreased glomerular filtration rate



Renal

Cellular damage

- Compromises filtration, reabsorption, secretion

Postrenal

Obstruction

- Urine unable to drain adequately

Prerenal - Hypoperfusion

Cardiogenic shock

Hemorrhage

Sepsis

Renal - Direct damage to kidneys

Toxins

Drugs

Infections

Hypoperfusion

Postrenal - Obstruction of urinary tract

Enlarged prostate

Kidney stone

Tumor

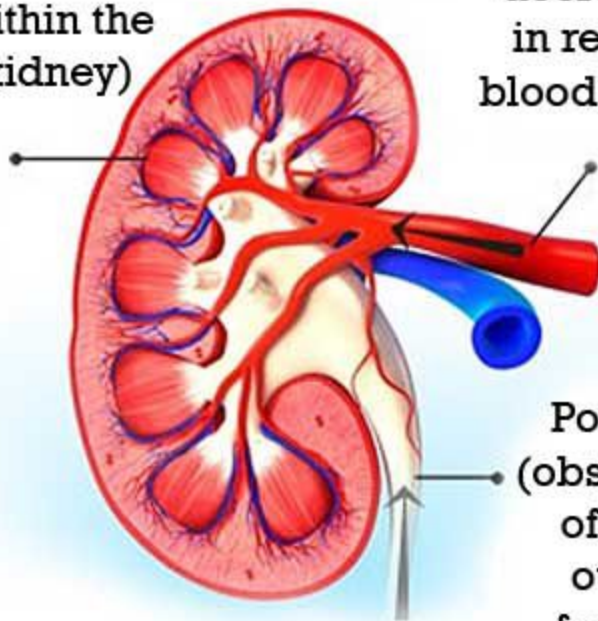
Trauma

Prerenal	Renal	Postrenal
Volume depletion	Vascular • Thrombotic thrombocytopenic purpura (TTP); hemolytic uremic syndrome (HUS)	Urinary tract obstruction • Ureteral obstruction • Bladder neck obstruction
Decreased effective circulation • Sepsis • Heart failure • Cirrhosis	Glomerulonephritis Acute interstitial nephritis (AIN) Acute tubular necrosis (ATN)	

Types of Acute Renal Failure

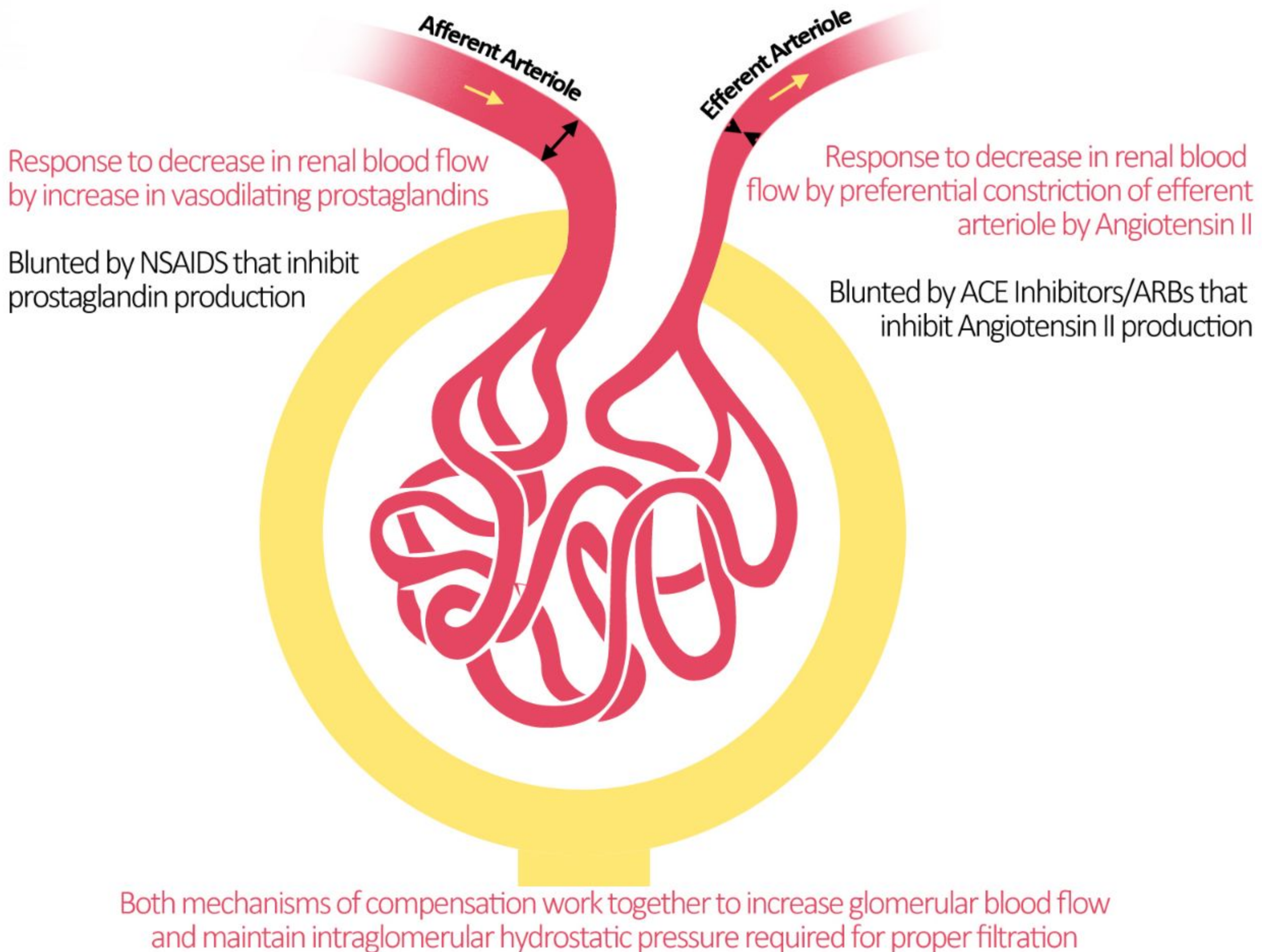
Intrinsic
(damage to
structures
within the
kidney)

Prerenal
(marked
decrease
in renal
blood flow)



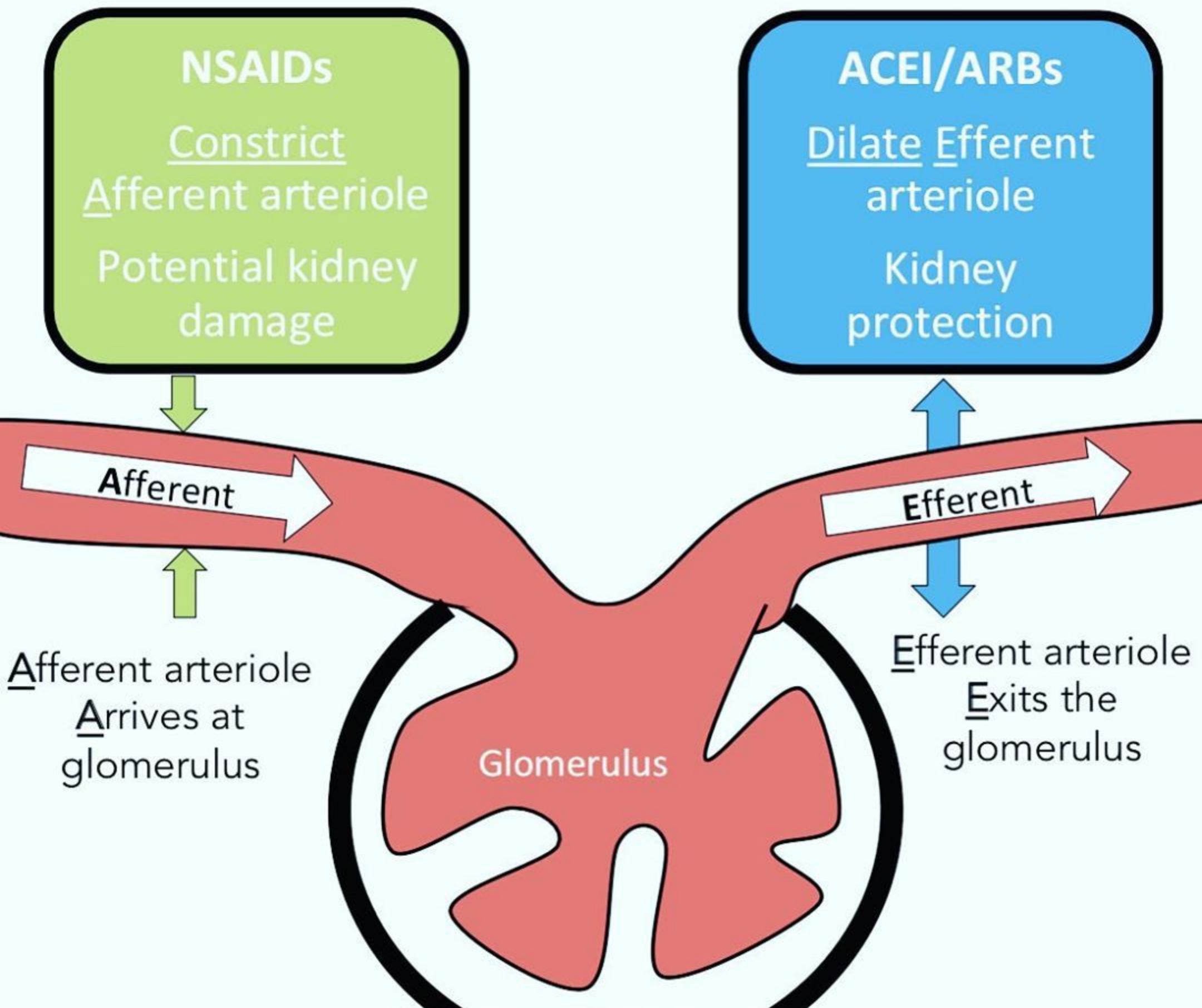
Postrenal
(obstruction
of urine
outflow
from the
kidney)

Pathophysiology of Prerenal AKI



Both mechanisms may be overcome by severe hypovolemia

NSAID vs ACEI/ARB on Kidneys



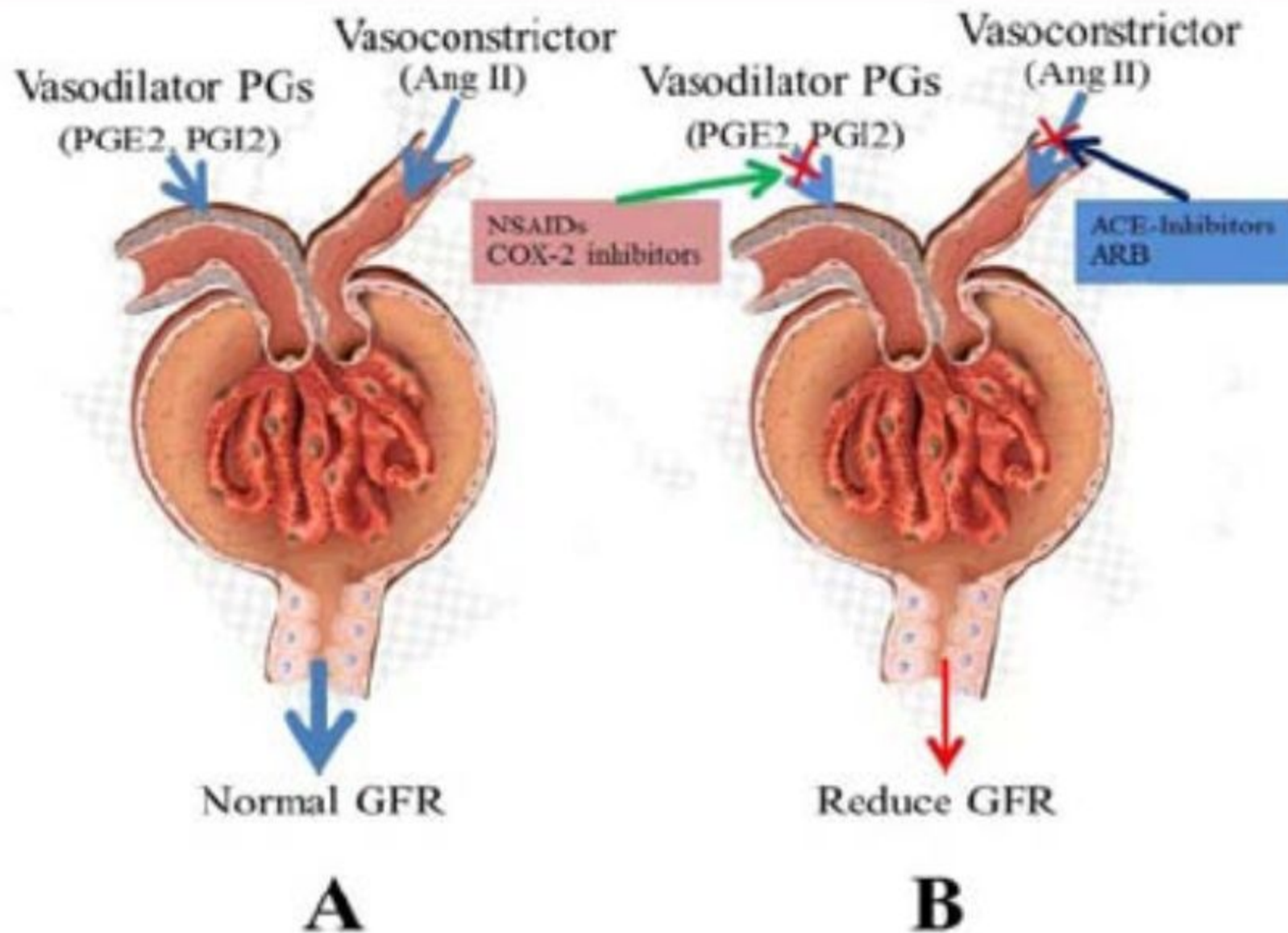
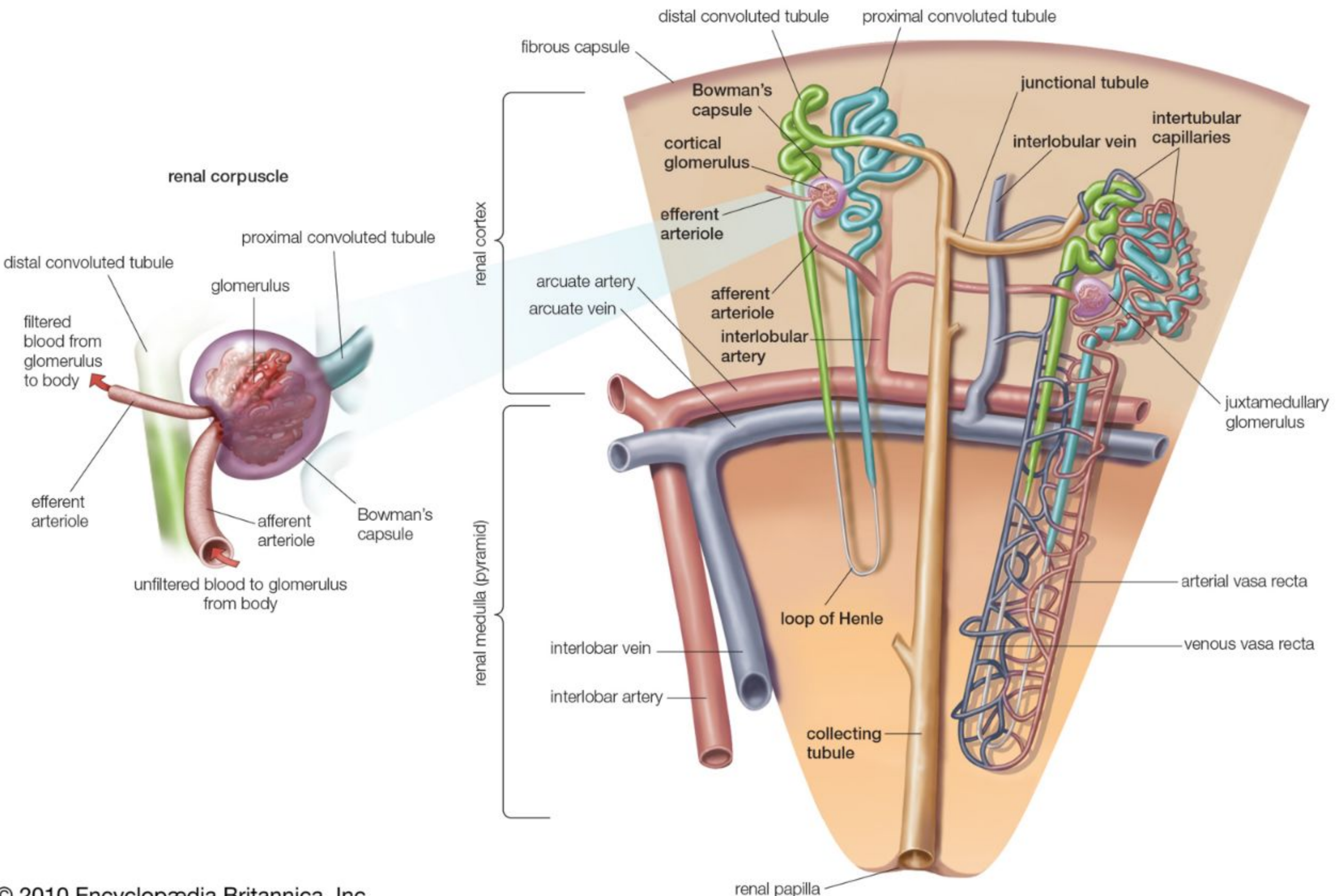


Figure 2: Regulation of renal blood flow & glomerular filtration in the kidney. PGE₂ and PGI₂ play an increasingly important role in maintaining renal perfusion by causing enhanced pre-glomerular vasodilation and angiotensin II (Ang II) produce efferent arteriole vasoconstriction to maintain normal GFR (A). Treatment by NSAIDs and COX-2 inhibitors can adversely affect renal function by blocking the production of autoregulatory prostaglandins resulting in a decline in GFR and treatment with ACE inhibitors or ARB can also further reduce glomerular perfusion and contribute to renal failure (B).



مبارح بدأنا بال Pre Renal AKI وشفنا ال causes اللي بتدخل المريض فيه
اليوم ان شاء الله رح نكمل ال Invisitation لل PreRenal ...

There are three major diagnostic approaches that, in the appropriate clinical setting, are used to distinguish prerenal disease from ATN and from other causes of AKI
عشان نعرف انه سبب ال AKI هو PreRenal في عنا 3 تحاليل بنقدر نعرف منها انه فعلا سبب ال AKI هو ال PreRenal ...
1●Urinalysis

2●Fractional excretion of sodium (FENa)

3●Response to fluid repletion in patients who have evidence of volume depletion, which is the gold standard for the diagnosis of prerenal disease

وفي عنا تحاليل مساعده للتشخيص زي :

4●Blood urea nitrogen (BUN)/serum creatinine ratio

5●Rate of rise of serum creatinine concentration

6●Urine osmolality

7●Urine volume

طبيب نيحي نفسر التحاليل هاي وشو رح نشوف فيها واحد واحد ٤٤٤

1●Urinalysis :

بندور هل في (Sediment(Cast

شو يعني cast

في عنا بروتين بال اسمه ال (THP) Tamm-Horsfall protein

is a glycoprotein produced exclusively by renal tubular epithelial cells within the distal loop of Henle, and it is one of the most abundant urine proteins

لو صار أي تغيير بال Kideny Environment زي مثلا تغيرت ال Acidity وال Electrolyte هادي التغيرات بتخلي ال THP يصيرله dwnaturation وتتغير طبيعته ويصير Sticky material اي حاجه نازله تلزق فيه

في ال Urineanalysis في ال PreRenal بيكون

normal or near normal in prerenal disease

الا اذا كان المريض عنده بالأصل Renal Disease ف ممكن يكون ال urinalysis بهلحاله Upnormal

يبقى بال PreRenal بيكون Normal

وممكن نلاقي

Hyaline and/or fine granular casts may be seen, but these are not an abnormal finding

اما لو كان السبب (ATN Renal) بيكون ال Urinalysis بيكون Upnormal وبنلاقي ساعتها في نوع من انواع ال Cast المميز

اسمه muddy brown granular, epithelial cell casts

رح نحكي عنه بالتفصيل لما نوصل لل ATN ان شاء الله
يبقى الخلاصه انه ال Urinalysis بيكون طبيعي وهاد اللي بيخليني أشك انه سبب ال AKI هو PreRenal
على عكس ال Renal ATN بيكون ال Urinalysis ع الاغلب غير طبيعي وفيه نوع مميز من ال ... cast

2● Fractional excretion of sodium (FENa)
FENa is the preferred test

$$\text{FENa, percent} = \frac{\text{UNa} \times \text{SCr}}{\text{SNa} \times \text{UCr}} \times 100$$

The urine-sodium concentration tends to be low in prerenal disease (less than 20 mEq/L) in an appropriate attempt to conserve sodium and high in ATN (more than 40 to 50 mEq/L) due, in part, to impaired tubular function induced by the tubular injury

في ال PreRenal بيكون ع الاغلب السبب hypovolemia والدم الواصل للكلى قليل ،، يبقى ال Na الواصل برده قليل
فيكون ال Urine Na قليل
the urine-sodium concentration in hypovolemic states should be less than 20 mEq/L

فلما يكون ال Na اقل من 20 , ونعوض بمعادله ال FENa
بتطلع النسبه أقل من 1%

Among patients with AKI, the FENa is typically less than 1 percent in prerenal disease (indicative of sodium retention)

اما بال ATN الخل بال Tubule مش قادره تعمل Reabsorption للصوديوم فال Na رح ينزل بكميات كبيره بال Urine

والصوديوم
the urine-sodium concentration in ATN (more than 40 to 50 mEq/L) due, in part, to impaired tubular function induced by the tubular injury
وبيكون ال FENa اكثر من 2%

3● Response to fluid repletion:

The gold standard for the distinction between prerenal disease secondary to volume depletion and postischemic or nephrotoxic ATN is the response to fluid repletion

لو كان سبب ال prerenal AKI هو ال hypovolemia واخذ المريض الكميّه المناسبه من ال Fluid
وبداً ال SrCr يقل خلال 24-72 ساعه
معناته السبب PreRenal

4● Blood urea nitrogen (BUN)/serum creatinine ratio
بال PreRenal AKI بيكون ال Bun/srCR اعلى من الطبيعي
Normal Bun/SrCr is 10:1 or 15:1

بال preRenal النسبه بترفع ل 20:1
due to the increase in the passive reabsorption of urea that follows the enhanced proximal reabsorption of sodium and water

5●Rate of rise of serum creatinine concentration

A slower rate of rise with periodic downward fluctuations (due to variations in renal perfusion) is suggestive of prerenal disease. 6●Urine osmolality

بال يكون ال Tubule لساته يشتغل منيح وقادر يعمل
Urine concentration

urine osmolality above 500 mosmol/kg is highly suggestive of prerenal disease since it reflects both the hypovolemic stimulus to the secretion of antidiuretic hormone and the maintenance of normal tubular function

7●Urine volume

The urine volume is typically, but not always, low (oliguria) in prerenal disease due to appropriate increases in both sodium and water reabsorption, which limits further fluid loss

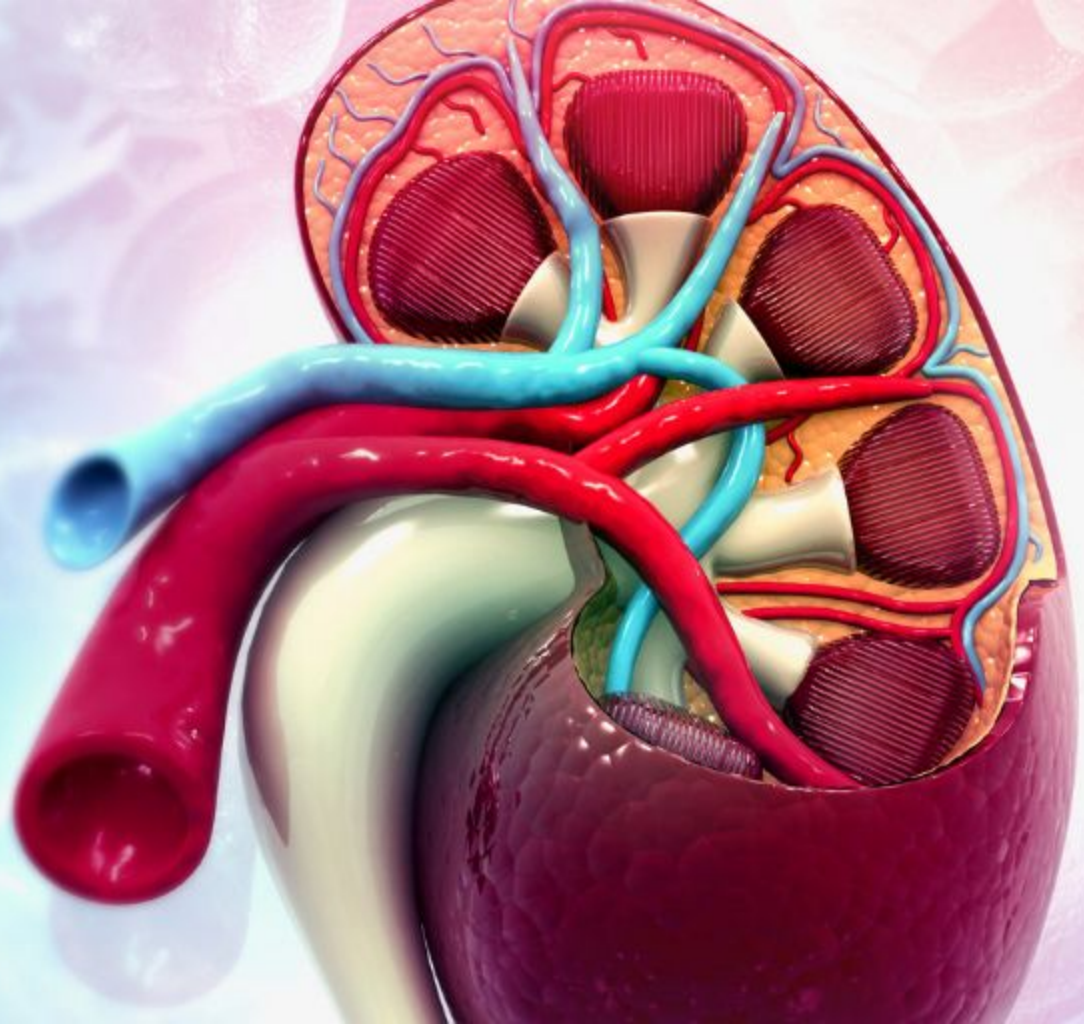
هيك بنكون وصلنا لنهايه ال Invisitation واهم شي مع هادي التحاليل نشوف ال History تبع المريض لو عنده
hypovolemia

او ماشي ع أدويه بتعمل PreRenal AKI

المره الجايه رح نتكلم عن ال

Pre Renal AKI Clinical Picture and Managment

#لعلي أفيدك ٤٤



Laboratory Test	Prerenal AKI	Intrinsic AKI	Postrenal AKI
Urine sediment	Hyaline casts, may be normal	Granular casts, cellular debris	Cellular debris
Urinary RBC	None	2–4+	Variable
Urinary WBC	None	2–4+	1+
Urine Na (mEq/L or mmol/L)	<20	>40	>40
FE _{Na} (%)	<1	>2	Variable
Urine/serum osmolality	>1.5	<1.3	<1.5
Urine/S _{cr}	>40:1	<20:1	<20:1
BUN/S _{cr} (urea/S _{cr} , SI)	>20 (>80)	~15 (~60)	~15 (~60)
Urine specific gravity	>1.018	<1.012	Variable

AKI, acute kidney injury; BUN, blood urea nitrogen; FE_{Na}, fractional excretion of sodium; S_{cr}, serum creatinine; RBC, red blood cell; WBC, white blood cell.

^aCommon laboratory tests are used to classify the cause of AKI. Functional AKI, which is not included in this table, would have laboratory values similar to those seen in prerenal AKI. However, the urine osmolality-to-plasma osmolality ratios may not exceed 1.5, depending on the circulating levels of antidiuretic hormone. The laboratory results listed under intrinsic AKI are those seen in acute tubular necrosis, the most common cause of intrinsic AKI.

تكلما المره الماضيه عن ال AKI Invistigation وكيف بنقدر من ال history للمريض وال Tests نتوقع انه سبب ال AKI هو pre Renal

اليوم رح نكمل مع ال Clinical picture وال Managment لل AKI PreRenal ..

زي ما قلنا بالبوستات السابقه مريض ال AKI PreRenal غالبا اما عنده

□ Kideny Hypoperfusion
OR
□ Drug induce nephrotoxcisty

لو كان Drug induced فهاد رح نعرفه لما نسال المريض عن الادويه اللي بياخدوها (ACEIs ,ARBs,NSAIDs)

والحل هنا انه نوقف الدوا المسبب لل AKI ..

ولو كان Hypoperfusion ممكن سبب من الاسباب

□ Volume depletion : 1
(vomiting, diarrhea, bleeding), renal losses (diuretics, glucose osmotic diuresis), skin or respiratory losses (insensible losses, sweat, burns), and third space sequestration (crush injury or skeletal fracture).
شو رح نشوف اعراض ع المريض ؟

اعراض ال ... Hypovolemic

Low BP ,low venous pressurecdry skin and mucosa ...

□ Shock Induce Hypotension
زي ال Septic ,Cardiac ,Hypovolumsic ..

والحل : نعالج ال Shock
وشفنا سابقا علاج ال septic shock بتفاصيلها ...

□ Heart Fauiler decreas cardiac out put and kideny perfusion

.. Edematous ويكون المريض

□ طيب نشوف كيف بنعالج ال Hypovolemic patients

□ Intravenous fluid therapy should be administered to patients with a clinical history consistent with

fluid loss (such as vomiting and diarrhea), a physical examination consistent with hypovolemia (hypotension and tachycardia), or oliguria

ال IV Fluid بنعطيه ع حسب حالة المريض كالتالي :

1□ If hypovolemia is confirmed by clinical assessment, we administer 1 to 3 liters of crystalloid (preferably buffered crystalloid) with assessment of clinical response. For volume responsive patients with a robust response in urine output and improvement in GFR, and with persistent evidence of hypovolemia or inability to maintain fluid balance, we continue maintenance isotonic fluids at 75 mL/hour or greater depending upon the ongoing losses

يعني لو المريض عنجد Hypovolemic بنعطيه من لتر ل 3 لتر
وبنشوف ال Response تبعه ،، لو بيستجيب ولساته Hypovolemic
بنكمل معه maintainance تقريبا 75ml بالساعة او اكثر حسب قديش بيفقد .. fluid

2□ Among patients with AKI who have a volume status that is difficult to interpret, such as in older adult patients or patients with reduced effective arterial blood volume, we administer a smaller volume trial (up to 1 liter) of an isotonic fluid. Based upon the response, a decision regarding continuation of fluid therapy may be made

مريض مش واضح عنده اذا كان Hypovolemic او لا
بنعطيه لتر وبنشوف ال Response □ لو ال Urineoutput تحسن وبدأ يزيد وبدأ ال srcr يقل بنكمل ... Fluid

3□ Patients who do not respond to administered volume with an increase in urine output or a decrease in the serum creatinine are unlikely to have prerenal disease and are more likely to have established Interensic AKI

.Continued volume expansion in these patients after a fixed initial trial is discouraged

لو المريض ما استجاب ع ال Fluid ف هون ممكن يكون مش prerenal

وسبب ال AKI هو Renal Causes فما بنكمل ع ال Fluid

عشان ما يدخل ب Fluid Overload

4□ Patients with conditions such as acute pancreatitis, rhabdomyolysis, or tumor lysis syndrome may require more liberal fluid resuscitation regimens

مثلا مريض ال Pancreatitis ممكن يحتاج

ml/kg/hr IV fluid 10-5

لو كان المريض anuric و ما في اي

evidence of volume overload

او فيه اي دليل على ال hypovolemia أو hypotension

بنديله fluid challenge ممكن 250 مل و يشوفه لو استجاب و بدأ يجيب Urine يبقى هاد غالبا pre renal failure نتيجة

hypo perfusion وبنكمل معه ...

يبقى الخلاصه علاج ال PreRenal AKI بنعالج السبب وبنوقف الادويه ال Nephrotoxic

ولازم نشوف لو في اي Complication زي ال

Electrolyte or acid base disturbance

ونصحها ...

#لعلِّي أفيدك ٩

How Acute Renal Failure Is Treated



IV fluids



Halting certain medications or supplements



Electrolyte management



Dialysis



TREATMENT

PRERENAL AKI WITHOUT FLUID OVERLOAD

- Intravenous fluids
- Volume status may be monitored with the use of a central venous catheter to avoid over- or under-replacement of fluid.

↓BP IN THE FLUID-REPLETE PATIENT

- Inotropes such as Norepinephrine & Dobutamine
- While a useful pressor, there is no evidence to suggest that Dopamine is of any specific benefit and may be harmful.

تكلما بالبوستات السابقة عن ال AKI

بدأنا بال Defenition وعرفنا انه عشان نحكي عن المريض دخل ب AKI لازم يكون عنده وحده ع الاقل من ال criteria التاليه :

1□ a rise in serum creatinine of at least 0.3 mg/dL (26.5 micromol/L) over a 48-hour period

2□ Srcr rise ≥ 1.5 times the baseline value within the seven previous days

3□ urine volume ≤ 0.5 mL/kg per hour for six hours
وبعدها شفنا تقسيمات ال AKI وال Stages حسب ال

RIFLE criteria ,AKIN criteria ,KDIGO criteria

وبعدين تكلما عن ال Causes وقسمناها ل

Pre Renal causes ,,Internsic causes ,,Post renal causes

ودخلنا بتفاصيل ال PreRenal وقلنا غالبا سببها Hypovolemia
وشفنا ال Investigation لالها

وعلاجها انو اعالج السبب ،فلو كان Hypovolemia رح أقيم ال
Volume status

و لو كان Hypovolemia رح نعطي fluid وفصلنا قديش رح اعطي
Fluid Responsiveness measurement حسب ال

ولو كان سبب ال preRenal هو Drug induced ساعتها بنوقف الادويه وبنقيم بردو ال Volume status ...

اليوم ان شاء الله رح نشوف النوع الثاني من ال AKI

□ Internsic AKI (Renal) □

Intrinsic - In response to cytotoxic, ischemic, or inflammatory insults to the kidney, with structural and functional damage

بال Kideny tissue Damage يكون صار Interensic AKI

خلل بأي Structure من النيفرون سواء ال

Glomerulus□□

او

Tubular tissue □□

واشهر شي ال ATN

او

Intersitial □□

واشهر سبب ال Acute Intersitial nephritis

□□Vessel

وهاد ال damage خلى النيفرون يفقد وظيفته وتتراكم ال waste product بالجسم ويدخل المريض ب AKI

طبيب نيجي نعمل ملخص للاسباب اللي بتعمل : Interinsic AKI

vascular (large- and small-vessel) causes of intrinsic AKI include the following:

1 Renal artery obstruction - (Thrombosis, emboli, dissection, vasculitis)

2 Renal vein obstruction - Thrombosis

3 Microangiopathy - (TTP, HUS, disseminated intravascular coagulation (DIC), preeclampsia)

4 Malignant hypertension

5 Scleroderma

6 renal crisis Transplant rejection

7 Atheroembolic disease

اي سبب من الاسباب السابقة ، بتأثر ع ال Kideny vessel

وبتأثر ع ال blood flow سواء الدم الداخلى او اللي خارج من الكلية

يعني مثلا بال Renal artery obstruction أولها رح يكون Prerenal ولو صلحنا السبب بسرعه بنمنع ال Internsic damage

لكن لو صار في Prolonged PreRenal faulter خلايا الكلية ما رح يوصلها الاوكسجين وال Nutrition وبالتلي بتدخل ب Ischemia و Necrosis

Glomerular causes include the following:

1 glomerulonephritis

غالبها سببها Immunity causes

Interstitial causes include the following:

1 Drugs - Penicillins, cephalosporins, NSAIDs, proton-pump inhibitors, allopurinol, rifampin, indinavir, mesalamine, sulfonamides

2 Infection - Pyelonephritis, viral nephritides

3 Systemic disease - Sjögren syndrome, sarcoid, lupus, lymphoma, leukemia, tubulonephritis, uveitis

ال Interstitial nephritis او غالبا بيسموها

Drug induce hypersensitivity intersitial nephritis

يعني اهم سبب لل intersitial nephritis هو ال Drug allergy

مثلا مريض اخذ pencillin وعمل له immune rxn في ال Intersitial وال Tubule

Tubular (Acute Tubular Necrosis ATN)

etiologies may include ischemia or one of the following :

1- cytotoxicity. Cytotoxic etiologies include the following:

Drugs - Aminoglycosides, lithium, amphotericin B, Vancomycin , pentamidine, cisplatin, ifosfamide, radiocontrast agents

2- Crystals - Tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate

3- Heme pigment - Rhabdomyolysis, intravascular hemolysis

الهيموجلوبين Toxic ع ال Tubule

اشهر سبب لل Internsic AKI هو ال (Tubular ATN)

اللي بيصير بال ATN

انه ال Ischemia او ال Toxin رح يعملو necrosis لل Tubular tissue

وال Tubular tissue رح توقع في ال lumen

وتلاقي بطريقها ال (THP Tamm-Horsfall protein) الموجود بال lumen

بتروح خلايا ال tubule بتلرزق بال THP

وبتعمل

muddy brown granular, epithelial cell casts

هاد ال cast ببسد ال Tubule

والميه الماشيه بال Tubule بتصير مش قادره تعدي من ال Tubule لل lumen

فما يبضل الا طريق واحد تروح عليه الميه المتجمعه بال Tubule

وهو ال blood [peritubular plexus] ال blood [peritubular plexus]

فكل الميه اللي بتتجمع بال Tubule رح ترجع لل blood

عشان هيك اغلب مرضى ال ATN بيكونو oligurea و hypervolemia

البوست القادم رح نكمل مع ال Internsic AKI

#لعلي_أفيدك ٤

Causes of AKI

Pre renal

Decrease in effective blood volume.
Arterial occlusion
Or
stenosis.
Hemodynamic Form.

Intrinsic renal

Vascular
Vasculitis.
Malignant
hypertension

Acute
Glomerulo
nephritis

Acute
Interstitial
nephritis

Acute
Tubular
necrosis

Ischemic.

Nephrotoxic.

Exogenous
Antibiotic
Radio contrast
cisplatin

Endogenous
Intra tubular pigment
Intra tubular protein.
Intra tubular crystal.

Post renal

Obstruction
Of
Collecting
System
Or
Extra renal
drainage

جمعه مباركه ٢٢

بدأنا مبارح بال Internsic AKI

وشفنا شو الاسباب اللي بتدخل المريض فيه

اليوم رح نكمل مع ال Invisitation اللي بتبين انه المريض عنده
ATN

رح تكون نفس ال Invisitation اللي شفناها بال PreRenal

وزي ما قلنا في عنا ثلاث تحاليل اساسيه بقدر منها اتوقع سبب ال AKI هل هو preRenal او Renal (ATN)

There are three major diagnostic approaches that, in the appropriate clinical setting, are used to distinguish prerenal disease from ATN and from other causes of AKI

1●Urinalysis

بال Urinalysis بحالات ال ATN بنلاقي نوع مميز من ال cast

muddy brown granular, epithelial cell casts

طيب هل وجود ال muddy brown granular, epithelial cell casts ,معناته اكيد المريض عنده ATN ??

وهل عدم وجود هاد النوع من ال cast معناته ننفي وجود ATN??

the absence of these Cast does not exclude ATN, and their presence does not always establish the
diagnosis of ATN

مثلا في حالات ال ATN البسيطة مش ضروري يكون صار necrosis كافي لانه يكونلي ال muddy cast

patients with less severe disease and nonoliguric ATN, a setting in which the urinalysis may be relatively normal

patients with higher urinary bilirubin levels had large numbers of granular casts and renal tubular epithelial cells on urine sediment, regardless of the presence of AKI

ففي حالات ال hyperbilirubinemia بنلاقي في

muddy brown granular, epithelial cell casts

بدون ما يكون في ATN

XXXXXXXXXXXXXXXXXXXX

2●Fractional excretion of sodium (FENa)

في حالات ال ATN ال Tubule بيكون فقد القدره على انه يعيد امتصاص الصوديوم

بالتالي الصوديوم بينفقد بال Urine

In ATN The urine-sodium concentration tends to be (more than 40 to 50 mEq/L) due, in part, to impaired tubular function induced by the tubular injury

وال (FENa) بيكون % 2 above in ATN

UNa x SCr

FENa, percent = ————— x 100

4● Blood urea nitrogen (BUN)/serum creatinine ratio The BUN/serum creatinine ratio is normal at 10 to 15:1 in ATN (measured in mg/dL) but is often greater than 20:1 in prerenal disease due to the increase in the passive reabsorption of urea that follows the enhanced proximal reabsorption of sodium and water

5● Rate of rise of serum creatinine concentration

The serum creatinine concentration tends to rise progressively and usually at a daily rate greater than 0.3 to 0.5 mg/dL (26 to 44 micromol/L) per day in patients with ATN. A slower rate of rise with periodic downward fluctuations (due to variations in renal perfusion) is suggestive of prerenal disease.

6● Urine osmolality

Loss of concentrating ability is an early and almost universal finding in ATN, with the urine osmolality being below 450 mosmol/kg in almost all cases and usually below 350 mosmol/kg. In contrast, a urine osmolality above 500 mosmol/kg is highly suggestive of prerenal disease since it reflects both the hypovolemic stimulus to the secretion of antidiuretic hormone and the maintenance of normal tubular function. However, lower values similar to those in ATN may be seen in prerenal disease and are therefore of little diagnostic help.

7● Urine volume

The urine volume is typically, but not always, low (oliguria) in prerenal disease due to appropriate increases in both sodium and water reabsorption, which limits further fluid loss. One exception is effective diuretic therapy, which will acutely raise the urine volume while the diuretic is acting.

In comparison, patients with ATN may be either oliguric or nonoliguric

هيك بنكون خلصنا ال ATN investigation

#لعللي أفيدك ٤

- Increase in serum Cr by ≥ 0.3 mg/dL within 48 hours
or
- Increase in serum Cr to ≥ 1.5 times baseline within the past 7 days
or
- Urine output < 0.5 mL/kg/hr for 6 hours

Common causes: **dehydration**, shock, heart failure, **BPH**, cirrhosis, **nephrotic syndrome**, glomerulonephritis, medications (NSAIDs, ACEI, ARB)

Initial evaluation: history and physical with an emphasis on the assessment of volume status, serum creatinine, **blood urea nitrogen (BUN)**, electrolytes, urinalysis, urine osmolality and sediment, and fractional excretion of **sodium (FENa^{*})**; if obstruction is suspected, renal ultrasonography and postvoid residual with bladder scan or catheterization

Prerenal: decreased renal perfusion (70% of community-acquired cases of AKI)
Urine sediment: bland, few hyaline casts
Serum **BUN**: creatinine $> 20:1$, urine osmolality > 500 mOsm (concentrated)
FENa: $< 1\%$ * (with exceptions)
FEUrea: $< 35\%$ (use if patient on diuretics)

Intrinsic:
Serum **BUN**: creatinine $< 20:1$
FENa: $> 2\%$ *
Urine osmolality: variable (< 450 mOsm)
Urine sediment: variable depending on etiology

Postrenal/obstructive:
Hydronephrosis
Postvoid residual > 100 mL
Urine sediment: bland, few hyaline casts, possible **RBCs**

Immediate relief with catheterization

Glomerular: **nephrotic syndrome**, glomerulonephritis
Interstitial: acute **interstitial nephritis (AIN)**, infiltrative process
Tubular/acute tubular necrosis (ATN): medication- or contrast-induced, toxin-mediated, prolonged hypotension
Vascular: microvascular, macrovascular, atheroembolic disease

Intravascular volume depletion:
weight loss, orthostatic hypotension, tachycardia, poor skin turgor
Dehydration/poor PO intake
GI losses: emesis, diarrhea
Hemorrhage
Renal losses: osmotic diuresis with hyperglycemia, diuretics
Insensible losses: perspiration, **burns**
Large vessel disease: **aortic** dissection, emboli
Abdominal compartment syndrome

Decreased effective arterial volume:
Sepsis/shock: evidence of infection, hypotension, acidosis, leukopenia or leukocytosis, tachycardia, tachypnea, constitutional symptoms
Heart failure: JVD, **pulmonary** edema, S₃, peripheral edema
Cirrhosis: **hepatorenal** syndrome, **ascites**, spider angiomas
Nephrotic syndrome: **proteinuria**, hypoalbuminemia, facial and peripheral edema

Selective renal ischemia:
Bilateral renal artery stenosis: possible history of hypertension, atherosclerosis, fibromuscular dysplasia/worsened by ACE inhibitors or ARBs
Arterial thrombus
Emboli

Medications affecting autoregulation
NSAIDs: vasoconstriction of afferent arterioles
COX-2 inhibitors: vasodilation of efferent arterioles
ACEI/ARBs
Calcineurin inhibitors: vasoconstriction of afferent arterioles

*FENa = $(\text{Na} - \text{Ur} \times \text{Cr} - \text{P}) / (\text{Na} - \text{P} \times \text{Cr} - \text{Ur}) \times 100$;
FENa $< 1\%$ is seen in contrast nephropathy and pigment nephropathy (rhabdomyolysis), both of which cause intrinsic renal failure. FENa can be $> 1\%$ with diuretics if overdiuresis is severe and also if prerenal failure develops in patients with CKD.

Laboratory Test	Prerenal AKI	Intrinsic AKI	Postrenal AKI
Urine sediment	Hyaline casts, may be normal	Granular casts, cellular debris	Cellular debris
Urinary RBC	None	2–4+	Variable
Urinary WBC	None	2–4+	1+
Urine Na (mEq/L or mmol/L)	<20	>40	>40
FE _{Na} (%)	<1	>2	Variable
Urine/serum osmolality	>1.5	<1.3	<1.5
Urine/S _{cr}	>40:1	<20:1	<20:1
BUN/S _{cr} (urea/S _{cr} , SI)	>20 (>80)	~15 (~60)	~15 (~60)
Urine specific gravity	>1.018	<1.012	Variable

AKI, acute kidney injury; BUN, blood urea nitrogen; FE_{Na}, fractional excretion of sodium; S_{cr}, serum creatinine; RBC, red blood cell; WBC, white blood cell.

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Exceptions in the evaluation of Urinary diagnostic indices in AKI

■ Pre-Renal Azotemia with High FeNa

- Diuretic therapy
- Chronic Kidney Disease
- Glycosuria (High osmolarity of urine)
- Alkaline urine

■ Low FeNa but NOT Pre-Renal

- Early stages of Obstruction
- Acute Glomerulonephritis
- Pigment Nephropathy
- Radio-contrast Nephropathy



FENa

<1%

Pre-renal

Severe renal vasoconstriction

HRS, NSAID

Disease of Afferent Arteriole

TTP, Scleroderma

Sepsis*

Nephropathy

Early myoglobinuric ARF

Acute Glomerulonephritis

Early obstructive uropathy

10-15% of non-oliguric ATN

>1%

Diuretic Use **wait 6 hrs**

Non-reabsorbable Solute

bicarbonate **also drags Na**

glucose **drives Na out**

mannitol

Mineralocorticoid deficiency

Late obstructive uropathy

Chronic Kidney Disease

ATN

Severe Ischemic

نكمل مع ال clinical picture of ATN

مرضى ال ATN يمر ب 3phases
(Oligurea phase) 1

acute decrease in (GFR) to very low levels, with a corresponding sudden increase in serum creatinine and blood urea nitrogen (BUN) concentrations most commonly 1-2 weeks

غالبا سبب ال ATN هو ischemia : ischemia رح تعمل injury

لل Tubular cell خاصة ال

....proximal tubules and in the thick ascending limb of the loop of Henle

طبيب شو اللي بيدخل المريض ب Oligurea

1- Ischemia lead to hypoperfusion ➔ decrease GFR
➔Decrease urineoutput

2-Presence to muddy brown granular, epithelial cell casts causing back-leak of filtrate through the damaged epithelium

هادي ال Cast بتسد ال Tubule وبالتالي ال urine مش رح يعرف يعدي ،فال Filtrate بيروح يعدي من ال Injured tubule ويرجع للدم

فيقل ال Urineoutput

3-Vasoconstriction

لما يكون ال Tubule متعور ،فالجسم بيحاول يقلل ال workload

على ال Injured kidney فيصير Autoregulation وافراز ل

ال leukotrine وغيرها من ال mediator اللي بتعمل V.C لل Renal artery وبالتالي بيقل ال GFR وبيقل ال Urineoutput

فنتيجة الميكانيزمات السابقة رح يكون المريض Oligurea
وغالبا طالما oligurea فالمية رح تتحوش بالجسم ويظهر عليه

⬜⬜ Hypervolemic Sign ⬜⬜

يعني عنده volume زياده على ال Circulation ⬜فيكون

Congested pulsated Neck vein⬜

⬜Secondary Hypertension

Hypertension encephalopathy ⬜ يمكن يوصل ل

⬜Pulmonary edema

⬜Confusion ,convulsion ,Coma

وسببهم ال Water Intoxication , زياده المية ع خلايا المخ بيصيرلها Swelling + زياده ال Urea بالدم

ولو وصل ل Uremic encephalopathy فلازمه Dialysis

+Hyper K

ال Tubule مش قادر يخرج ال K من الجسم فبيتراكم ..

Metabolic Acidosis

وسببها انه ال tubule مش قادر يخرج ال H+ ولا قادر يعيد امتصاص ال HCO₃ ولا قادر يصنع ال HCO₃

Note

Hyperkalemia lead to acidosis ,and Acidosis lead to hyperkalemia

Uremic Syndrom

اهم ما يميز ال ATN هو ال Uremic Syndrom

الكلية مش شغاله والمكونات اللي كان لازم تنزل بال Urine مش هينزلو وهيقعدو بالدم يبقى ال Uremia باختصار يعني مكونات ال Urine صارت بالدم

شو الاعراض اللي بتكون مصحوبه ب Uremic Syndrom ...

1- Anorxia ,Nausea ,Vomiting

جهاز ال GIT اكثر جهاز عنا حساس لل Toxin ..

فارتفاع ال Toxin في الدم بتعمل Irritation لل GIT

2- Bleeding Tendency

بس غالبا بتكون مع ال Chronic renal faulter (CRF)

(3- Pruritus (Itching

ال Toxin بيعمل Skin Irritation

4- pleurisy & Pericarditis

ولو وصل المريض لهادي المرحله يبقى لازم Dialysis

5- Coma ,confusion ➔ Indication for dialysis

ثاني phase بيمر فيه المريض هو ال

(Polyuric Phase)

بهاي المرحله بيكون ال Tubule بدأ يخف وبيصير يطلع كميات كبيره من ال Urine ممكن توصل ل 5-10 لتر

وبيصير عند المريض

hypotension ,dehydration ,Electrolyte loss

بس هاي المرحله مؤقتة وسرعان ما يدخل المريض بالمرحلة الثالثة

The recovery phase

بترجع ال Kideny للوضع الطبيعي وبالتالي ال Volume وال Electrolyte بترجع لل Normal

ال ATN بتعتبر Reversible والمريض بيخف تلقائي ،بس الأهم انه نحافظ عليه Stable ونمنع ال progressive complication

فبصلح ال volume status وال Electrolyte

البوست القادم رح نشوف ان شاء الله كيف التعامل مع حالات ال ATN

#لعلي_أفيدك ٤

Ischemia

Vasoconstriction

Tubular Damage

Direct Glomerular
Effect

Obstruction by
Casts

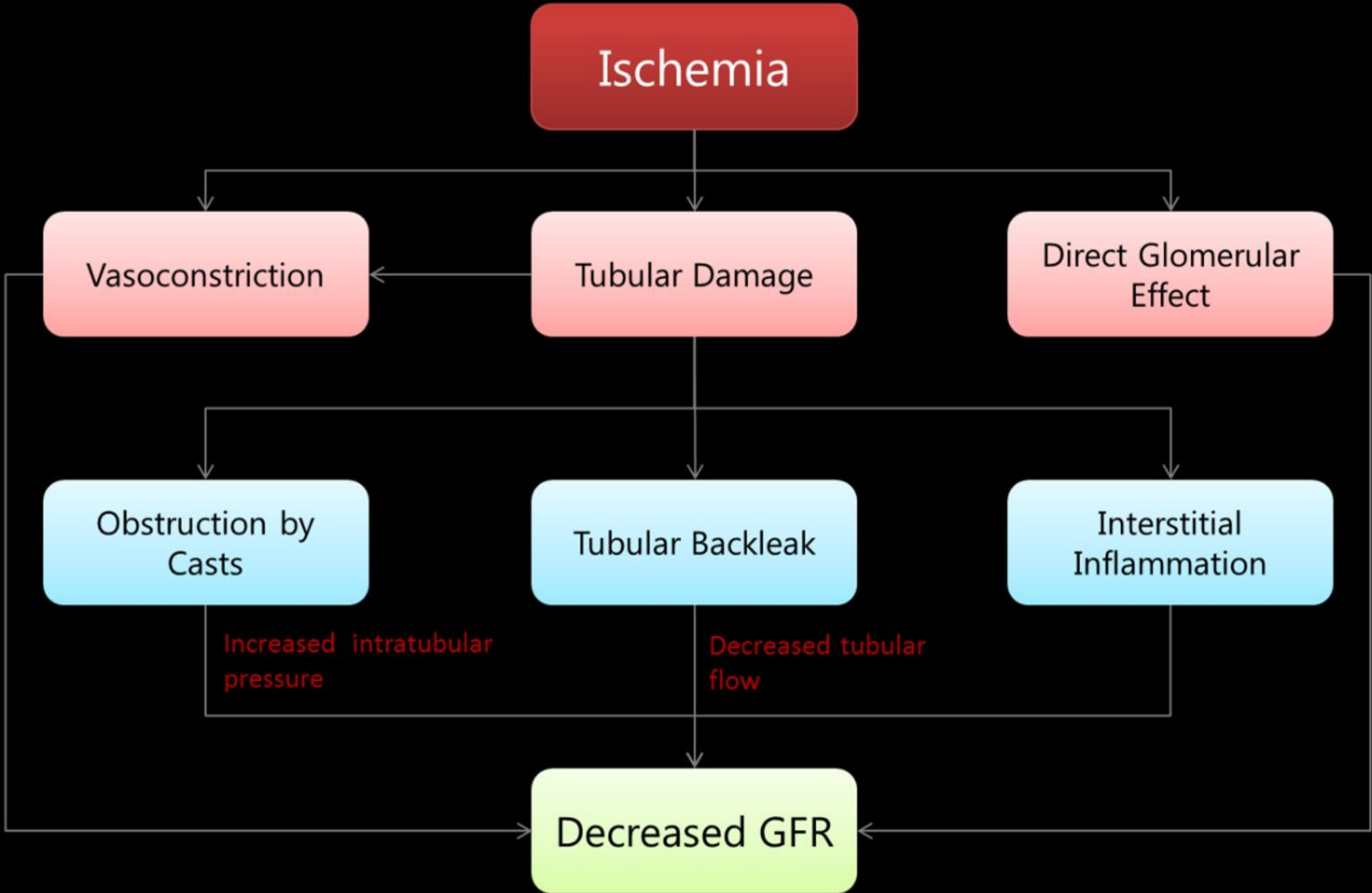
Tubular Backleak

Interstitial
Inflammation

Increased intratubular
pressure

Decreased tubular
flow

Decreased GFR



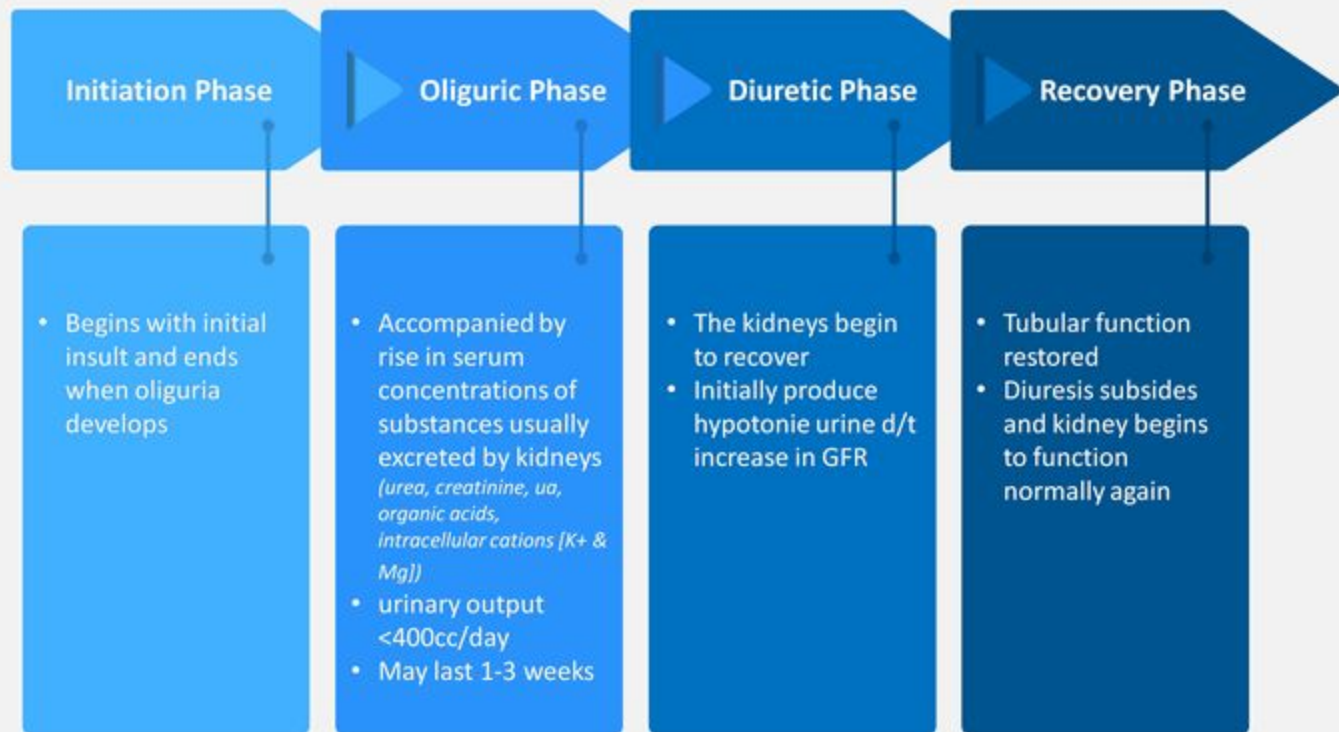
Phases of Acute Renal Failure

- Clinical progression of reversible RF occurs in four phases:
 - **Initiation phase**
 - Begins with initial insult and ends when oliguria develops
 - **Oliguric phase**
 - Accompanied by rise in serum concentrations of substances usually excreted by kidneys (urea, creatinine, ua, organic acids, intracellular cations [K^+ & Mg])
 - urinary output $<400\text{cc/day}$
 - May last 1-3 weeks
 - **Diuretic phase**
 - The kidneys begin to recover
 - Initially produce hypotonic urine d/t increase in GFR
 - **Recovery phase**
 - Tubular function restored
 - Diuresis subsides and kidney begins to function normally again

RENAL FAILURE

Phases of Acute Renal Failure

Clinical progression of reversible RF occurs in four phases



وقفنا المره الماضيه عند ال ATN investigation

Management of ATN ال نكمل مع ال

اتفقنا أن ال AKI ← يعتبره Reversible ورح ترجع الكليه

لطبيعتها بعد فتره من الوقت

بس أهم شي بهادي الفتره يضل المريض Stable ونمنع ال Complication

وعرفنا كمان انه غالبا مريض ال ATN بيكون Oligurea و Hypervolemia

وممكن يكون عنده مشاكل بال Electrolyte زي ال K+

وتغيرات بال Acid- base balancs ...

بس لو رجعنا وتذكرنا ال PreRenal كان بردو المريض Oligurea

بس غالبا معاه Hypovolemic sign ... عشان هيك بنبدأه ب

....Fluid resuscitation

طيب لو كان المريض oligurea وعنده احد العلامات التاليه : ...

1- Fail to be adequately resuscitated

2- Persistent oliguria

3- Doubtful that a fluid/vasopressor/inotrope challenge would help ...

بهادي الحالات بنلجأ ل Test اسمه FST

Furosemide Stress Test

ال FST بيقول انه لو عندك مريض Oligurea وبك تفرق هل هو prerenal ولا ATN بنعطي المريض

1.5mg/kg/Lasix-1

If the pateint doesn't Recive a loop diuretic day 1-7 befor the test ➡➡ so give him 1mg Lasix /kg

If the pateint Recive a loop diuretuc within 1-7 day befor the test ➡➡ so give the pateint 1.5 mg lasix/kg

وبعد ما ياخذ المريض ال Lasix , بنشوف ال Urineoutput(U.O) وبناء على ال U.O بنحدد اذا كانت PreRenal او ATN

لو كان ال Urineoutput اكثر من 200ml خلال ساعتين من اعطاء ال Lasix معناها ال Tubule شغاله تمام والحاله prerenal ←←

وبنعوضه Fluid

-then Attempt further hemodynamic

□

لو كان ال Urineoutput اقل من 200 ml خلال ساعتين من اعطاء ال Lasix معناها ال tubule مش قادره تستجيب لل Lasix والسبب لل Oligurea هو ATN

وال ATN غالبا رح يكون Hypervolemic

٤٤٤ فلو كان المريض Oligurea & Hypervolemic كيف بيكون التعامل معه

٤ اول شي نعرف شو اللي بيخلي المريض Hypervolemic

1□initial evaluation

المريض جاي من الاول ب Hypervolemic مع ال ATN
OR

2□occur due to excessive fluid administration in the setting of impaired ability to excrete sodium and water

OR

3□primary left or right ventricular dysfunction and lead to AKI (type 1 cardiorenal syndrome).

٤ طيب كيف رح نعالج مريض ال Hypervolemic...

Diuretics may be used to relieve hypervolemia among patients with AKI who are not anuric. Loop diuretics are the preferred agents as they provide a greater natriuretic effect than thiazide diuretics

For patients who are oliguric and hemodynamically stable, we use 80 to 200 mg of intravenous (IV) furosemide or equivalent and monitor for an increase in urine output

● In diuretic-naïve patients : 1□

لو المريض ما بياخد diuretic بنبدأ معه بجرعه
mg lasix IV 80
او ما يكافئ ال lasix من ال loop

يعني ممكن ياخد Bumetanide او Torsemide

□40 mg lasix = 10 mg Torsemide = 1 mg bumetanide

لو المريض بالاصل ماشي ع diuretic بنعطيه جرعه تكون ع الاقل مضاعفه للجرعه اللي هو بياخذها , يعني فرضا هو عنده Resistance HTN

وماشي ع 80 mg lasix مع ادويه الضغط التانيه

ودخل ب AKI وكان Hypervolemic , لازم جرعه ال lasix ما تقل عن 160 mg

طبيب كيف بنعرف انه المريض استجاب ع ال lasix ولا لا؟؟

بنراقب استجابته المريض لل diuretic حسب ال U.O

فلو المريض بيجيب urine بمقدار

0.5 - 1 ml/kg/hr

معناها في استجابته ع ال Diuretic وبنكمل معه

لو ما جاب هادي الكمية وكان unresponsiveness

ساعتها بنشوف طريقه ثانيه عشان نخلصه من ال Volume overload زي ال Ultrafiltration خصوصا لو كان وضعه Critical ..

يعني بنبدأ مع المريض ب 80 mg لو كان naive او جرعه اعلى لو كان هو بالابل ماشي ع Lasix ...

وبنشوف ال U.O , لو المريض جاب Urine بمقدار

1ml/kg/hr-0.5

يعني لو مثلا وزنه 80kg وبدأ ع 80 mg لازكس

وخلال اول ساعه كان ال U.O 65 ml/hr ← 0.8ml * 80 kg

(0.8ml * 80 kg = 65 ml/hr)

معناته في استجابته Responsiveness

طبعاً لو المريض Stable ووضعه كويس ، ما بقيس كل ساعه

ممکن نشوف الكمية خلال 6-12 ساعه

يعني بمشييه ع Lasix وبشوف ال U.O خلال 6-12 ساعه

لو كان المريض بيجيب 1ml/kg/hr-0.5 معناته بيستجيب ع ال Lasix وبنكمل معه ع Continuous Infusion وبنراقب ال

UO لحد ما يوصل المريض لل Normal volume اما لو كان المريض مش Stable وخايفين يدخل ب Pulmonary edema

مش هنستنى 6 ساعات ، ممكن نشوف ال U.O خلال ساعه او ساعتين ، لو بدا يستجيب منيح ووضعه بدأ يتحسن بنكمل ع

Diuretic

لو ما استجاب او كانت استجابته ضعيفه ووضعه مش Stable ساعتها بيلجأو لل Dialysis as Ultrafiltration

XXXXXXXXXXXXXXXXXXXX

يبقى عنا احتمالين اما Response او No response

□□

لو المريض ما استجاب من اول IV bolus of lasix بنعمل مضاعفه للجرعه خلال اول ساعتين

If there is little or no response to the initial dose, the dose should be doubled at two-hour intervals, as needed, up to the maximum recommended doses

يعني لو مريض بدأ ع 80 mg لازكس وما استجاب ووضعه Stable

بنرفعله الجرعه ل 160 mg خلال اول ساعتين

(maximum of 200 mg in a single dose of IV furosemide or equivalent).

طبيب لو وصل لل Maxiumum dose بدون استجابته ولساته stable بنمشيه ع Continuous infusion مع ال Bolus مع

بعض

وينشوف هل استجاب او لا
Thiazide لو ما استجاب بنضيف

Addition of a thiazide diuretic such as metolazone or chlorothiazide (500 to 1000 mg IV) is sometimes given in conjunction with furosemide to augment urine output

□□Lack of response to a 200 mg dose of IV furosemide or equivalent, with or without a thiazide □□.diuretic, may suggest the need for extracorporeal removal of excess volume
اما لو المريض كان مش Stable و pulmonary edema مثلا وما استجاب او استجابته كانت ضعيفه لل First diuretic bolus
مش حنقعد نجرب معه , نظرا لانه وضعه غير مستقر بنلجأ لل
Ultrafiltration ..

□□
أما لو المريض استجاب من اول Bolus لل Lasix وكميه ال Urine output بتزيد ..

Among patients who respond to diuretics, we continue to give repeated doses to avoid hypervolemia .if kidney function is improving or improvement is thought to be imminent

المريض اللي بيستجيب ع أول bolus ولساته بده كمان diuretic
غالبا بيمشوا بعد اول bolus على Continuous infusion ويمكن يضل ع bolus عادي
حسب استجابته المريض

Continuous diuretic therapy may be less ototoxic than bolus therapy and maintains a sustained effective rate of diuretic excretion.

□A continuous infusion should only be used in patients who are first responsive to bolus loop diuretic therapy , Thus, in patients who fail to respond to the maximal bolus doses described above, □.continuous infusion will be ineffective

□ال bolus of lasix بينعطى slowly لتجنب ال Toxicity

•20 to 40 mg over five minutes

•60 to 120 mg over 20 minutes

(•160 to 200 mg over 40 to 50 minutes (4 mg/min

اما ال : Continuous infusion

●An IV loading dose of 40 to 80 mg of furosemide is typically given over five minutes prior to initiating the continuous infusion. If the patient has received one or more IV boluses within the previous few hours, then an infusion can be started without a loading dose.

●After the loading dose, the starting infusion rate with furosemide varies with the level of kidney :function

فحسب ال GFR بنعطي ال Dose

1□If GFR less than 25 ml/min

ب 20mg/hr Infusion ال ببداً

If the diuresis is not sustained, a second bolus is given followed by a higher infusion rate of 40 mg per hour

2□If GFR 25-75 ml/min

Dose 10-20 mg/hr

3□If GFR >75 ml/min

Dose 10 mg/hr

حسب ال UpToDate جرعه ال Infusion

1□If the patient has an eGFR greater than or equal to 30 mL/min

initial furosemide infusion rate of 5 mg per hour.

If the diuresis is not sustained, a second bolus is given followed by a higher infusion rate of 10 mg per hour. This rate may then be increased further to the maximum recommended furosemide infusion rate of 40 mg per hour if response to lower doses is poor.

2□If GFR less than 30 mL/min

we use an initial furosemide infusion rate of 20 mg per hour. If the diuresis is not sustained, a ...second bolus is given followed by a higher infusion rate of 40 mg per hour

وبنكمل مع المريض لحد ما يصير Normal volume ..

#لعللي أفيدك ٤

Diuretics in AKI :-

In hypervolumic patient with oliguria $\Rightarrow$ Use Diuretic



(A) In naive patient start with lasix at dose 80 mg

(B) Non naive patient start with lasix at dose that are at least double to the dose that patient is on it

then, check Response



goal Response is to obtain urine output $\Rightarrow$ 0.5-1 mL/kg/hr



IF NO Response
"and patient is stable"



increase the starting dose to the double within First 2 hour



IF NO Response
"and patient still stable"



add chlorothiazide
500 - 1000 mg I.V



If NO Response
shift to dialysis
"ultrafiltration"

If there's Response
and patient need more diuretic, shift to Continuous Infusion according patient

GFR

give Loading dose $\rightarrow$ 40 mg lasix then

GFR $> 75 \rightarrow$ 10 mg/hr

GFR 25-75 $\rightarrow$ 10-20 mg/hr

GFR $< 25 \rightarrow$ 20-40 mg/hr.



When patient is Euvolumic Stop

Diuretics....

Use of furosemide stress test to guide resuscitation ??

Appropriate candidate for furosemide stress test

- Felt to be adequately resuscitated
- Persistent oliguria
- Doubtful that a fluid/vasopressor/inotrope challenge would help



Furosemide stress test

- Furosemide naive: 1 mg/kg IV bolus
- Not furosemide naive: 1.5 mg/kg IV bolus



UOP >200 ml in two hours:
Passed furosemide stress test

Pre-renal oliguria



- Replace urine output
- Attempt further hemodynamic manipulation to improve urine output
- Urine output may be a useful measurement of organ perfusion



UOP <200 ml in two hours:
Failed furosemide stress test

Intrinsic renal failure



- Additional fluid, vasopressors, or inotropes are unlikely to improve urine output
- Urine output isn't a meaningful measurement of perfusion

Practical Diuretic Resistance Management

1st Step

Maximize IV loop
bolus doses

Have you reached the
ceiling dose?
Furosemide ~200 mg

Yes

2nd Step

Administer a
bolus PLUS
continuous IV
infusion

Failed Step 2?

Yes

3rd Step

Add metolazone or
chlorothiazide 30
minutes prior
diuretic

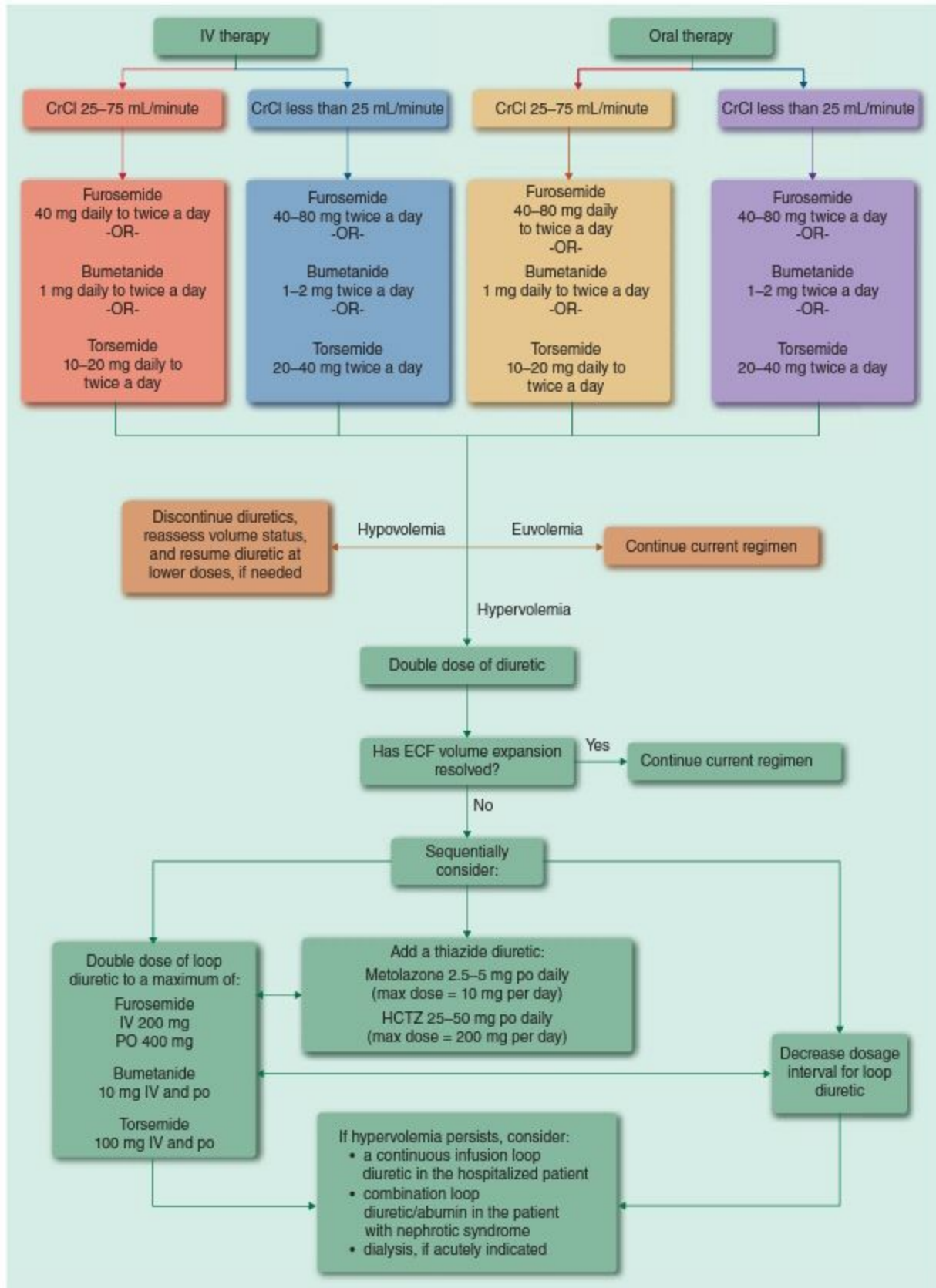
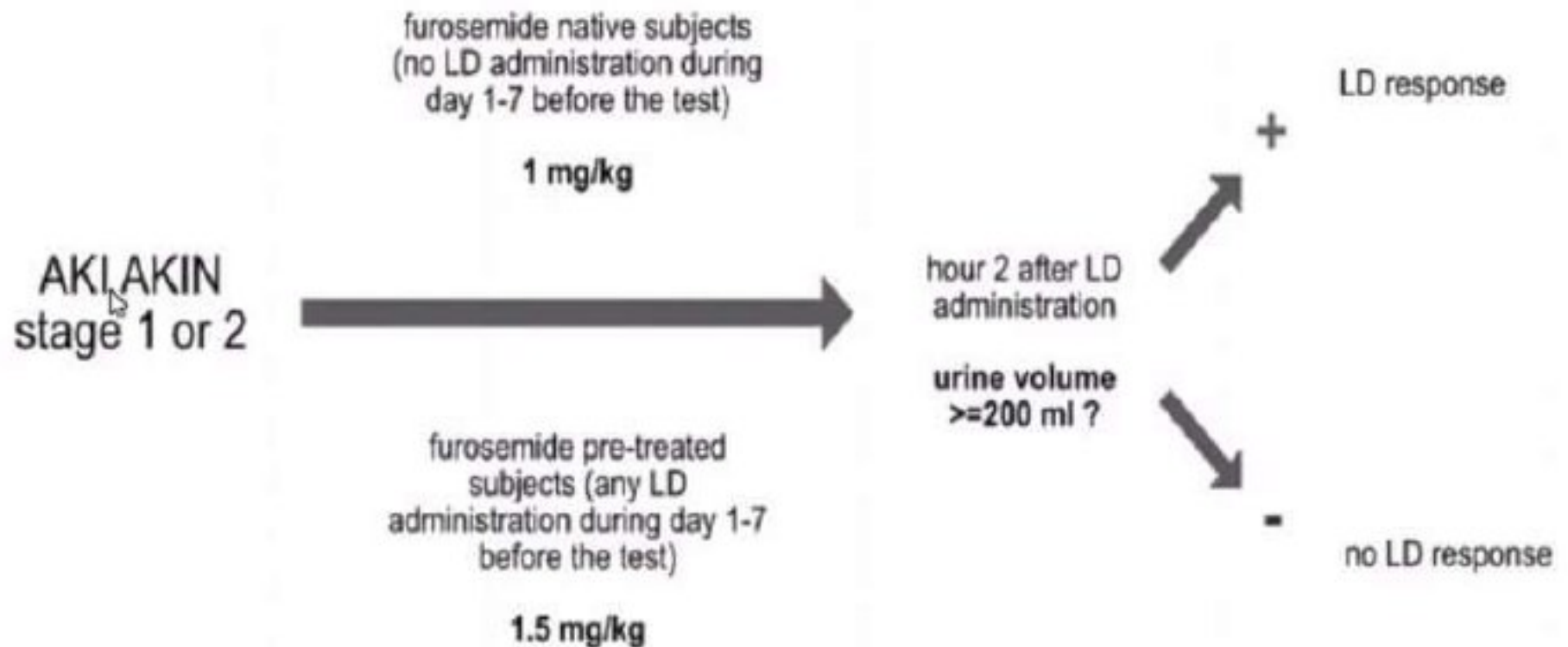


FIGURE 25-2. Algorithm for treatment of extracellular fluid expansion. (CrCl, creatinine clearance; ECF, extracellular fluid; HCTZ, hydrochlorothiazide; po, oral.)

Furosemide Stress Test "FST"

- Dosage of the drugs depends on whether subjects have received LD previously (day 1–7 before testing).
- UOP must be quantified until the next two hours after drug administration.
- A total volume of 200 mL or more (100 mL/h) indicates LD responsiveness.



Dosage Regimens For Continuous IV Diuretic Administration

Creatinine clearance (ml/min)	Loading dose (mg)	Infusion rate (mg/h)		
		<25	25-75	>75
Furosemide	40	20 then 40	10 then 20	10
Bumetanide	1	1 then 2	0.5 then 1	0.5
Torsemide	20	10 then 20	5 then 10	5

في البوست الماضي عرفنا انه مريض ال ATN
 غالبا يكون oligurea مع Hypervolumic ...
 وشفنا متى يستخدم ال Diuretic ونشوف هل في استجابه او لا ..

في بعض النقاط رح نزودها في ال Management ونشوف متى المريض يحتاج ... Dialysis

1- Districition to Fluid and Sodium ,and potassium

2- suggest achieving atotal energy intake of 20-30 kal/kg/day in patients with any stage of AKI
 (Grade 2C)

3-We suggest administration 0.8 to 1.0g/Kg/day protein in noncatabolic AKI patients without need
 for dialysis(Grade2D)

And 1.0-1.5g/Kg/day protein in patients with AKI on RRT(Grade2D)
 and up to a maximum of 1.7g/Kg/day protein in patients on CRRT and in hypercatabolic patients with
 AKI(Grade2c)

(4-We recommend ☐ not using low-dose dopamine or fenoldopam to prevent or treat AKI (Grade1A

لو في Complication بنصلحها زي ال
 Hyper K+
 Metabolic Acidosis

ورح نرفق ال Ttt لهاي ال complication باختصار مع الصور ..

طيب متى ب يكون المريض بحاجه ل RRT

RRT = Renal Replacement therapy (Dialysis) indication in AKI :

Refer the following life-threatening complications for emergency renal replacement therapy (RRT):

1- Refractory hyperkalaemia (potassium >6.5 mmol/L)

2- Refractory metabolic acidosis (pH <7.15)

3- Refractory volume overload with or without pulmonary oedema

4-End-organ complications of uraemia (e.g., pericarditis, encephalopathy, uraemic bleeding) or other
 end-organ involvement (e.g., neuropathy, myopathy)

.(5-Severe AKI and poisoning/drug overdose (e.g., ethylene glycol, lithium

Acute Kidney Injury



Indications for dialysis in patients with AKI



A
Acidosis



E
Electrolytes



/
Intoxications



O
Overload



U
Uremia

Indications Of Dialysis, In AKI



Summarized with the mnemonic "AEIOU":

Acidemia(intractable) from [metabolic acidosis](#) in situations in which correction with sodium bicarbonate is impractical or may result in fluid overload

Electrolyte abnormality, such as severe [hyperkalemia](#) $> 6.5-7$ mmol/L or with ECG changes. Temporize with calcium, D_{50} + insulin, HCO_3 , beta-agonist nebulizers, and kayexalate.

Intoxication, that is, acute poisoning with a dialyzable substance. These substances can be represented by the mnemonic SLIME: [salicylic acid](#), [lithium](#), [isopropanol](#), Magnesium-containing laxatives, and [ethylene glycol](#)

Overload of fluid not expected to respond to treatment with diuretics (intractable)

Uremia complications, such as [pericarditis](#), [encephalopathy](#), seizure, [gastrointestinal bleeding](#) or intractable nausea/vomiting.

****RRT In AKI:** Keep BUN < 100 mg/dl, Creat < 10 mg/dl.

Management of complications

Complication	Mangement
Hyperkalemia	.Calcium gluconate .Insulin and glucose .Beta2agonist(salbutamol) .Ion exchange resin. - Hemodialysis.
Acidosis	.IV or oral sodium bicarbonate if PH<7.1 - Hemodialysis if severe acidosis
Pulmonary edema	- If ventilatory failure:ventillation or intubation. .Diuretics(furosemide) .for decompansated heart, opoids,nitrates
Fluid imbalance	Normal saline for hypovolemic patients with prerenal AKI

رح نبدأ بال AKI_Prevention#

لو في عنا مريض herat fauiler ال srcr عنده 1.3 ورح يبدأ ب

ACEIs Or ARBs

مثلا بدأ كالتالي :

Lisinopril $\Rightarrow$ Oral: Initial: 2.5 to 5 mg once daily

و بعد 5 ايام من بدايه ال ttt ارتفع ال srcr ل 1.5

وضله stable ع 1.5mg/dl

وبعد اسبوعين رفعو الجرعه ل

mg once daily 20

وال srcr وصل ل 1.6 وضل ثابت ع هادي القيمه

هل المريض يكمل ع ال ACEIs ولا لاً ...

من المعروف انه ال ACEIs او ال ARBs بيعمل تثبيط لل Ang2

وبالتالي بيصير V.D لل blood vessel ومن ضمن ال vessel اللي رح يصيرها Dilatation $\Leftarrow$ هي ال Efferent arteriole

وحكيينا ببوست ال prerenal AKI انه ال VD لل Efferent

بيخلي الدم يطلع بسرعه من ال Glomerulus وبالتالي

Decreases in Intraglomerulus pressure $\Rightarrow$ decreases in GFR $\Rightarrow$ so Induce Functional (Hemodynamic mediated) AKI

فال ACEIs او ال ARBs بتعمل elevated in srcr خلال 2-5 يوم من بدايه اخذ العلاج ..

وهاد ال elevated بيكون Dose Dependent

يعني الجرعه العاليه رح تعمل Elevated srcr اسرع وبقيم اعلى

طيب شو هي ال Risk factor لل ACEIs renal toxicity

1-Bilateral renal artery stenosis

2-Effective blood flow as (CHF ,Cirrhosis)

3-preexisting kidney disease

4-Volume depletion (●Patients on high-dose diuretic therapy in whom there is relative hypovolemia (due to excessive diuresis

٤٠ عشان هيك أي مريض رح يمشي ع ACEIs او ARBs

لازم نعمله التالي لمنع ال AKI :

1-Start with alow dose

بنبدأ بجرعه قليله ،ونرفعها بالتدريج كل 1-2 اسبوع ...

2-switch to long acting ACEIs when tolerancs is established

يعني مثلا لو بدأ المريض ب Captopril اللي هو short acting ويتاخذ ثلاث مرات باليوم ،بنبدأ بجرعه صغيره وبالتدريج

بنرفع الجرعه لحد ما يوصل المريض ال Effect المطلوب Tolerated

بعدها ممكن نحوله ع اشي long actig زي ال Enalapril او ال ... lisinopril

3-Avoid using other Nephrotoxic drugs

4- Initially minitor Srcr weekly in outpatient

And daily in inpatient

ف رح نتابع ال srcr وبناء ع القيم رح نشوف هل المريض يكمل ولا يوقف العلاج ...

لو المريض بدأ ع lisinopril مثلا وال srcr ارتفع 30% عن ال Baseline

يعني كان زي المثال اللي ضربناه

كان 1.3mg/dl ووصل ل 1.6 (30+1.3%)

لحد 30% بيكون Acceptable ويتتابع المريض كل فتره ...

اما لو زاد عن 30% من ال baseline ➡➡ بنقل الجرعه للنص

ويتتابع المريض

لو بردو ضل زايد 30% عن ال baseline رغم تقليل الجرعه للنص بالتالي بيتوقف العلاج ويمشي المريض ع جروب ثانيه ما

تأثر ع الكلى

في حالات لو كان ال ACEIs هو الخيار الافضل وال Benefit اكثر من ال Risk زي حالات ال DM with proteinuria ممكن

تجاوزاا يوصل المريض ل 50% عن ال baseline ويمشي بنص ال dose

مع المتابعه المستمره

ف الاعتماد الاكبر والتطبيق حسب هل ال srcr ارتفع 30% عن ال baseline او لا وبناء عليه

اما بيستمر المريض في حال ما زاد عن 30%

او بنقل الجرعه للنص لو زاد عن 30% من ال baseline

او بنوقف الدوا لو ضل ال baseline اكثر من 30% رغم انه المريض ماشي ع نص الجرعه

From baseline (less applicable) %50

According to UpToDate

- the following changes in kidney function are generally considered acceptable:

An increase in serum creatinine of up to 50 percent above baseline

- The dose of the ACE inhibitor should be decreased by one-half, and the creatinine should be repeated in approximately one week, if any of the following occur:

- The serum creatinine increases to a level that is 50 to 100 percent above baseline

- The ACE inhibitor should be stopped, and specialist advice should be sought, if any of the following occur:

- The serum creatinine increases by more than 100 percent above baseline

#لعلي أفيدك ؟

**30–49% increase in creatinine or
25–50% decrease in eGFR**



- 1** Carefully consider a reduction (eg halving) of ACE/ARB/MRA dose and recheck
- 2** Critically examine diuretic dose
- 3** Look for any other potential nephrotoxins eg NSAIDs, PPIs etc

**≥50% increase in creatinine or
≥50% decrease in eGFR**



- 1** Stop ACE/ARB/MRA and recheck
- 2** Exclude renal artery stenosis
- 3** Critically examine diuretic dose
- 4** Look for any other potential nephrotoxins eg NSAIDs, PPIs etc

**FREQUENT MONITORING AND A MULTIDISCIPLINARY APPROACH
ARE ESSENTIAL IN THESE PATIENTS**

Starting ACE Inhibitors for Heart failure

Patient Presentation

- Confirmed Left Ventricular Systolic Dysfunction

GP

CAUTION

Seek specialist advice from heart failure nurse or cardiology if creatinine >200, urea >12, potassium >5.0, sodium <130, systolic BP <90, aortic stenosis Contraindicated in renal artery stenosis. See

<http://www.edren.org/pages/gpinfo/ace-inhibitors-how-to-start.php> for detailed advice.

INITIATION

NONE of these present- start ACEI
Ramipril 1.25mg or Lisinopril 2.5mg
consider
stopping NSAID or Potassium
sparing diuretic

TITRATION

Titrate dose slowly by doubling dose fortnightly
depending on renal function, monitor BP and check U&E, 1-2 weeks after each titration

MAINTAINENCE

- Aim for target doses (Lisinopril 20mg, Ramipril 10mg, or 5mg bd or highest tolerated dose)
- Remember some ACE is better than none
- Check for ADR- dizziness, cough, angioedema, URT symptoms

Renal Impairment?

Creatinine rise <50% from baseline acceptable if patient well
If >50% , consider stopping NSAIDs, reducing diuretics if no fluid retention

Problem Solving;

Potassium <5.5mmol/l acceptable on stable doses ACEI/Diuretic
Between 5.5-6mmols, recheck within 24 hours

- >6mmol/l stop ACEI., get cardiology advice
- >7mmol/l urgent referral to hospital
- **Symptomatic hypotension** – consider swapping to bedtime, consider reducing diuretic if no fluid overload or reconsider need for nitrates/calcium channel blocker.

Useful information for patients with confirmed LVSD

- Record daily weight
- Reduce salt intake to <2gms daily
- Early symptom recognition and reporting
- Importance of medication compliance
- Flu & Pneumococcal immunisations

ACE Cough?

- Confirm dry and tickly if Ace cough swap to ARB such as Candesartan or Valsartan
- If not consider/treat LRTI, pulmonary oedema,

مسا الخير ٤٤

بدأنا المره الماضيه مع ال

AKI_Prevention#

وبدأنا بال ACEIs وال ARBs

وعرفنا انه مجموعه ال ACEIs وال ARBs بتعمل

Functional mediated AKI (Prerenal) By Dilatation of the Efferent arteriole

وحكيانا عن القيم لل SrCr اللي مسموح المريض يوصلها ومتى بخلي الجرعه زي ما هي ومتى بنزل بالجرعه بالنص ومتى بنوقف

الدوا وبنشفط (Shift) المريض ع مجموعه تانيه

اليوم ان شاء الله رح نشوف ال NSAIDs effect on kideny

وكيف بتعمل AKI ... ♀♀

٤ بداية نتفق انه ال

Nonselective and Selective NSAIDs

اللاتنين الهم نفس ال Effect ع الكليه وما في فرق بيناتهم ٤٤٤٤...

خلينا نشوف شو نوع ال AKI اللي ممكن يصير بسبب ال NSAIDs

1 Acute kidney injury (hemodynamically (Functional)-mediated or acute tubular necrosis)

2 Acute interstitial nephritis

3 Nephrotic syndrome (minimal change disease or membranous nephropathy)

4 Hyponatremia

5 Hyperkalemia/type 4 renal tubular acidosis

6 Hypertension/edema

7 Acute papillary necrosis

8 Chronic tubulointerstitial nephritis/analgesic nephropathy

9 Uroepithelial malignancy

XXXXXXXXXXXXXXXXXXXX

خلينا نرجع لشغل ال NSAIDs وكيف بيأثر ع الكليه

زي ما بنعرف انه ال tissue cell membrane فيه PL (phospholipid)

بيشغل ع ال Phospholipid انزيم ال PLA2 (Phospholipade A2) لينتج عنا ال (A.A)Arachidonic Acid

وال Arachidonic acid بيشتغل عليه انزيمين ال COX وال LOX

ال COX يصنع ال (Prostaglandins PGs)

وال LOX يصنع ال leukotrein

PL $\Rightarrow$ PLA₂ $\Rightarrow$ A.A $\Rightarrow$ COX + LOX
COX $\Rightarrow$ PGs

بالكلية ال PL تبع ال Glomerulus يصنع PGE₂ & PGI₂

وال Vascular Endothelium وال Tubule وال Intersitial cell بتصنع ال PGE₂

طبيب شو وظيفه ال PGs بالكلية ٤٤

في ال Normal cindition ال PGs بتعتبر
Vasodilator

يعني بتخلي ال Afferent Aretry واسع ليدخل الكمية الكافية من الدم لداخل ال Glomerulus ويحافظ ع ال Filtration pressure

وبالتالي بنحافظ ع Normal GFR

اما ب Certain Condition زي مثلا حالات ال Hypotension او حالات ال Low renal perfusion زي مثلا مريض عنده heart faulter

او في حالات زياده افراز ال Norepinephrine او ال Ang 2

او ال Vasopressin او ال Endothelin اللي بيعملو V.C

فأى حاله بيصير فيها V.C لل vessel او قله ال Hypoperfusion
ال PGs رح يعمل سلسلة من ال Effects التاليه :

1 $\Rightarrow$ promot Secretion of Renin

2 $\Rightarrow$ Impair Na reabsorption in henle loope and collicting duct

3 $\Rightarrow$ Partially Antagonise the ADH

وهاي ال Effect رح نشوفها بالتفصيل مع ال NSAIDs Electrolyte change with

٤ يبقى باختصار في الحالات ال normal وظيفه ال PGs ك Vasodilation

اما بال Pathogen condition بيكون في Effect زياده ع ال Vasodilator effect

طبيب نرجع لل NSAIDs من المعروف انه الميكنازم لل NSAIDs

بتعمل تثبيط لل Prostaglandin synthesis

وبالتالي رح نفقد ال Vasodilator Effect وال Other Effect ...

XXXXXXXXXXXXXXXXXXXX

خلينا نشوف ا اول نوع من ال AKI ونكمل الباقي ع البوستات الجاية ان شاء الله ٤٤ :

... (1) Acute kidney injury (hemodynamically-mediated or acute tubular necrosis

تأثير ال NSAIDs بال Functional AKI

بسبب ال PGs inhibition رح يصير V.C لل Renal aretry وبالتالي رح تقل كميته ال blood الداخلة لل kidney وبالتالي يقل ال GFR وبالتالي يتتراكم ال waste producer ويرتفع ال SrCr

ال NSAIDs Functional AKI يظهر من اليوم ال 3 لل 7 من استخدام ال NSAIDs ويبداً ال srcr يرتفع

لو المريض ضل يستخدم ال NSAIDs ممكن يدخل ب Ischemia من ال Renal V.C ويدخل ب ... ATN

NSAID-induced inhibition of PG-mediated afferent vasodilation and reduction in peritubular blood flow may also increase the risk of ischemic acute tubular necrosis (ATN) or other nephrotoxin-induced tubular injury from drugs such as aminoglycosides, amphotericin B, hydroxyethyl starch, and radiocontrast material

مين اكثر واحد من ال NSAIDs بيعمل AKI ?

⊗ Indomethacin the potent one

اما ال NSAIDs اللي الها less AKI

هو ال Sulindac وال Low dose aspirin

طبيب مين الناس اللي عندهم Risk factor لل NSAIDs induce AKI

●Chronic kidney disease (CKD), especially stage 3 or worse (ie, estimated GFR [eGFR] <60 mL/min/1.73 m²)

●Volume depletion from aggressive diuresis, vomiting, or diarrhea

●Effective arterial volume depletion due to heart failure, nephrotic syndrome, or cirrhosis

●Older age ●Severe hypercalcemia with associated renal arteriolar vasoconstriction

كيف ممكن نعمل Prevention لل NSAIDs AKI

1) avoiding NSAIDs among high-risk patients (such as those with chronic kidney disease [CKD], volume depletion, heart failure, or hypercalcemia)

2) We suggest that the chronic use of NSAIDs be avoided chronic NSAID use (as defined as nearly every day for 30 days or longer) , if at all possible, among all patients with a reduced eGFR (ie, eGFR <60 mL/min/1.73 m²) and suggest cautious use in patients with even mild reduction (ie, eGFR 60 to 89 mL/min/1.73 m²) and other comorbid conditions or risk factors, including heart failure, cirrhosis, or nephrotic syndrome.

3) For patients with reduced eGFR in whom limited NSAID use is unavoidable (such as those with significant pain or mobility issues in whom other pain medications are significantly less effective),

the patient should be advised of the risk, and the creatinine should be followed closely when receiving NSAIDs.

4□ Patients should not receive NSAIDs prior to procedures involving radiocontrast or other nephrotoxic drug administration

طبيب فرضا المريض دخل بـ functional AKI كيف نعالجه؟

Stop NSAIDs -1

2- Reassess Fluid

ع الاغلب المريض بـ يكون عنده low urine volume بسبب ال V.C

يعني ممكن يكون Edematous

3- RRT if needed

وهيك بنكون شفنا اول نوع من ال NSAIDs AKI □

#لعللي_أفيدك □



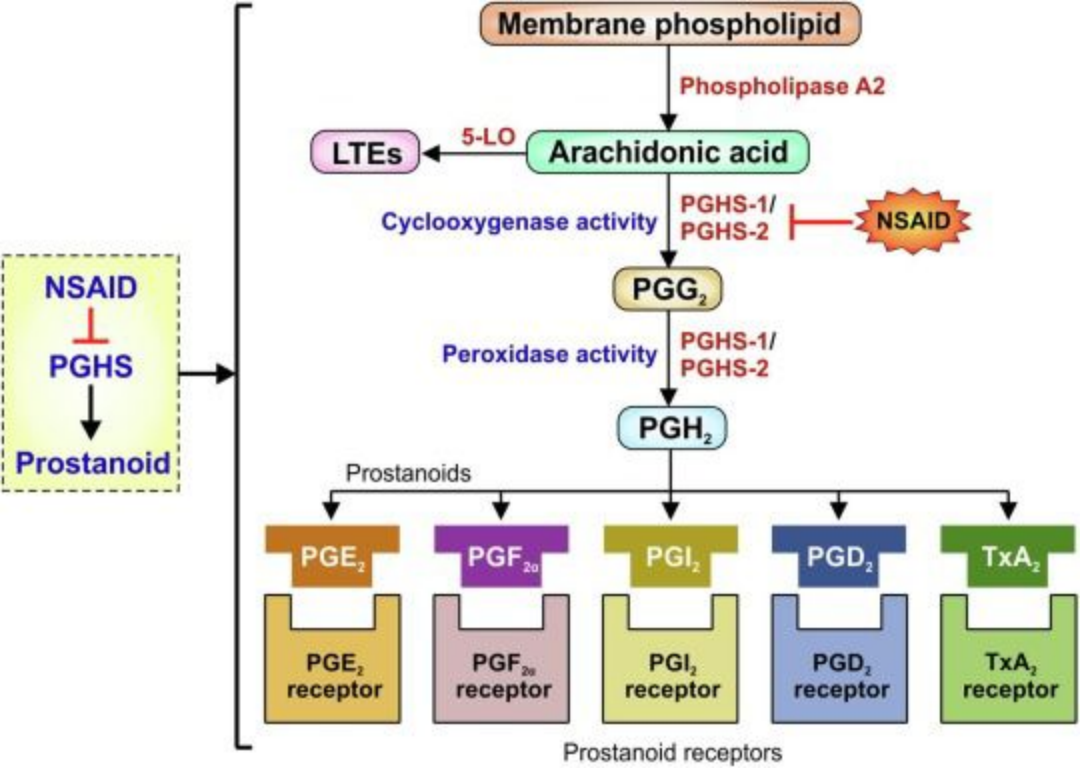
DANGERS OF **NSAIDS**

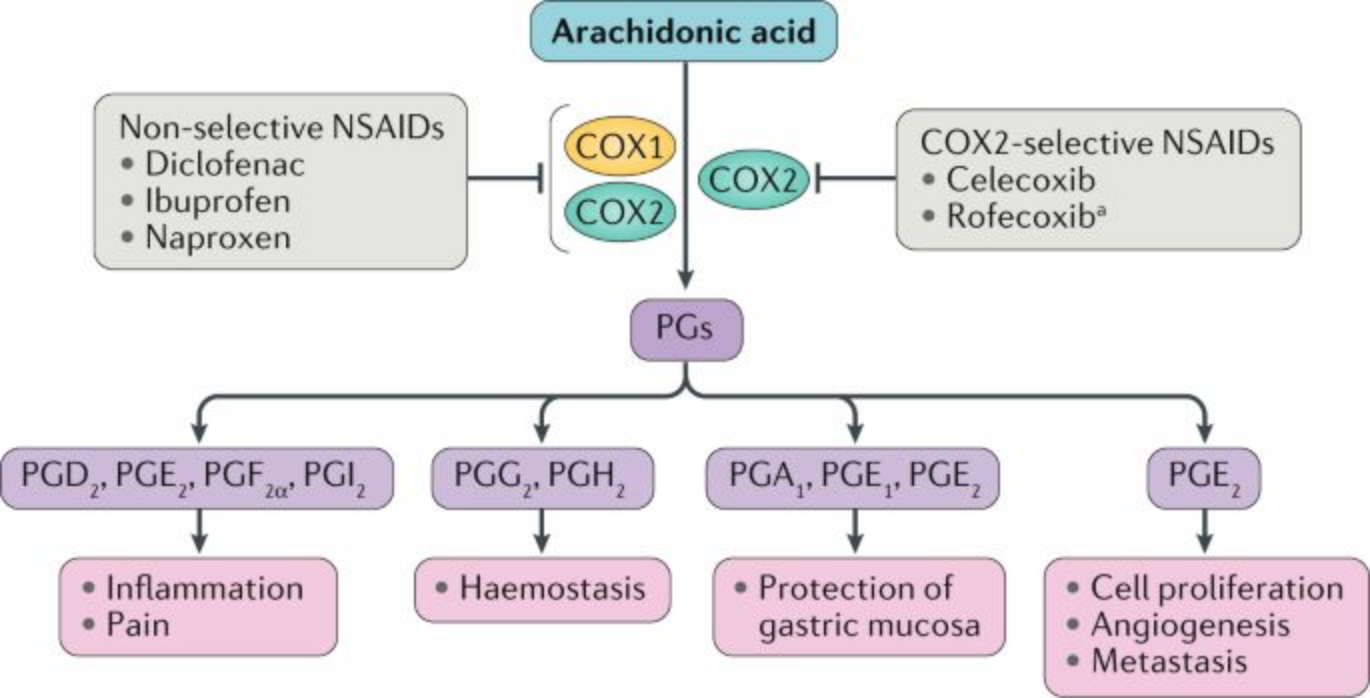
(non-steroidal anti-inflammatory drugs)



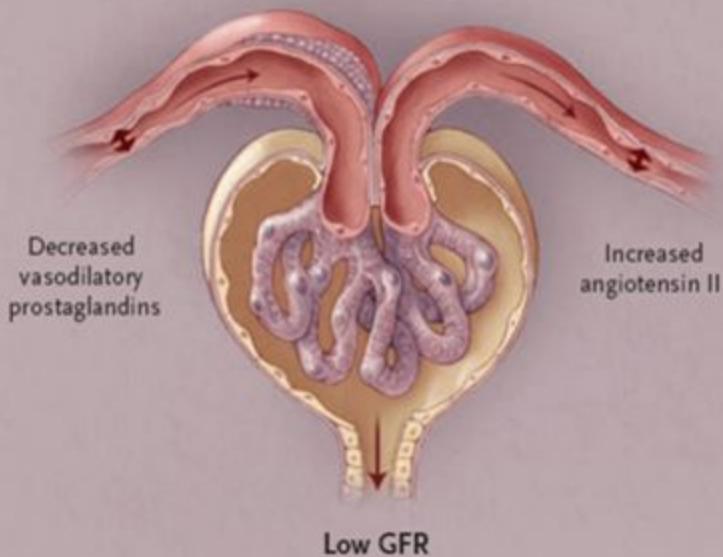
NSAID

A red and white capsule is shown horizontally, resting on a reflective surface. The capsule has a white left half and a red right half. The word "NSAID" is printed in black, bold, serif capital letters across the center of the capsule. The red half of the capsule has a small, faint, embossed mark that appears to be the letters "AS". The capsule is reflected on the surface below it.

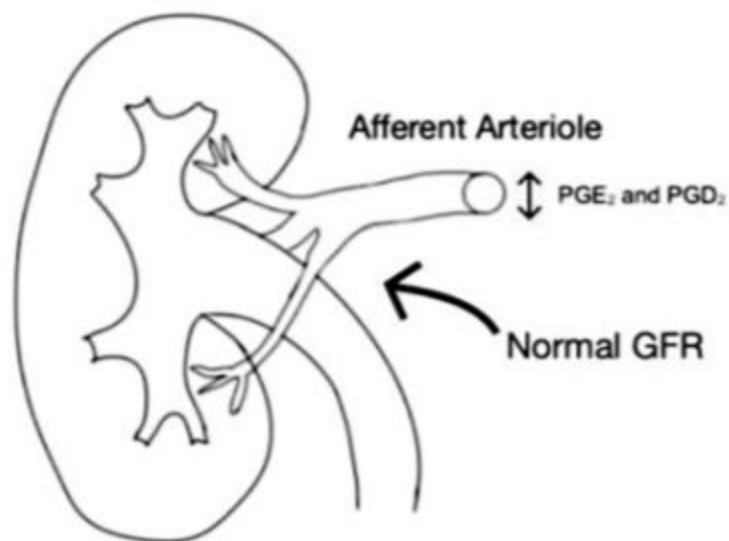




C Decreased perfusion pressure in the presence of NSAIDs

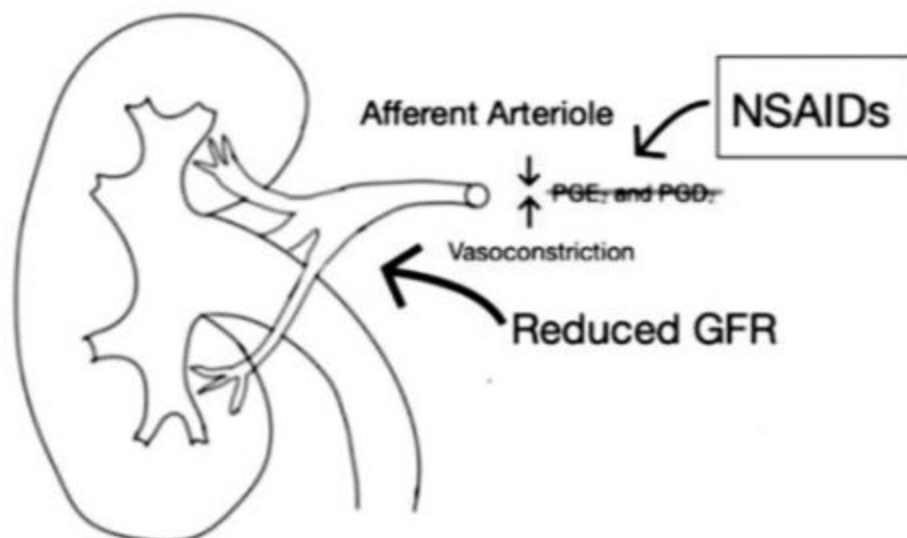


No NSAID Exposure



- In the non-NSAID exposure kidney pictorial, the afferent arteriole is adequately dilated by prostaglandins (PGE_2 and PGD_2).
- This dilation of the afferent arteriole allows for adequate renal blood perfusion.
- The kidney is able to maintain necessary filtration processes.

NSAID Exposure



- In the NSAID exposure kidney pictorial, the afferent arteriole is vasoconstricted due to prostaglandin (PGE_2 and PGD_2) inhibition.
- This vasoconstriction of the afferent arteriole restricts renal blood perfusion.
- This kidney is unable to maintain necessary filtration processes.

Figure 1. Mechanism of NSAID induced AKI.

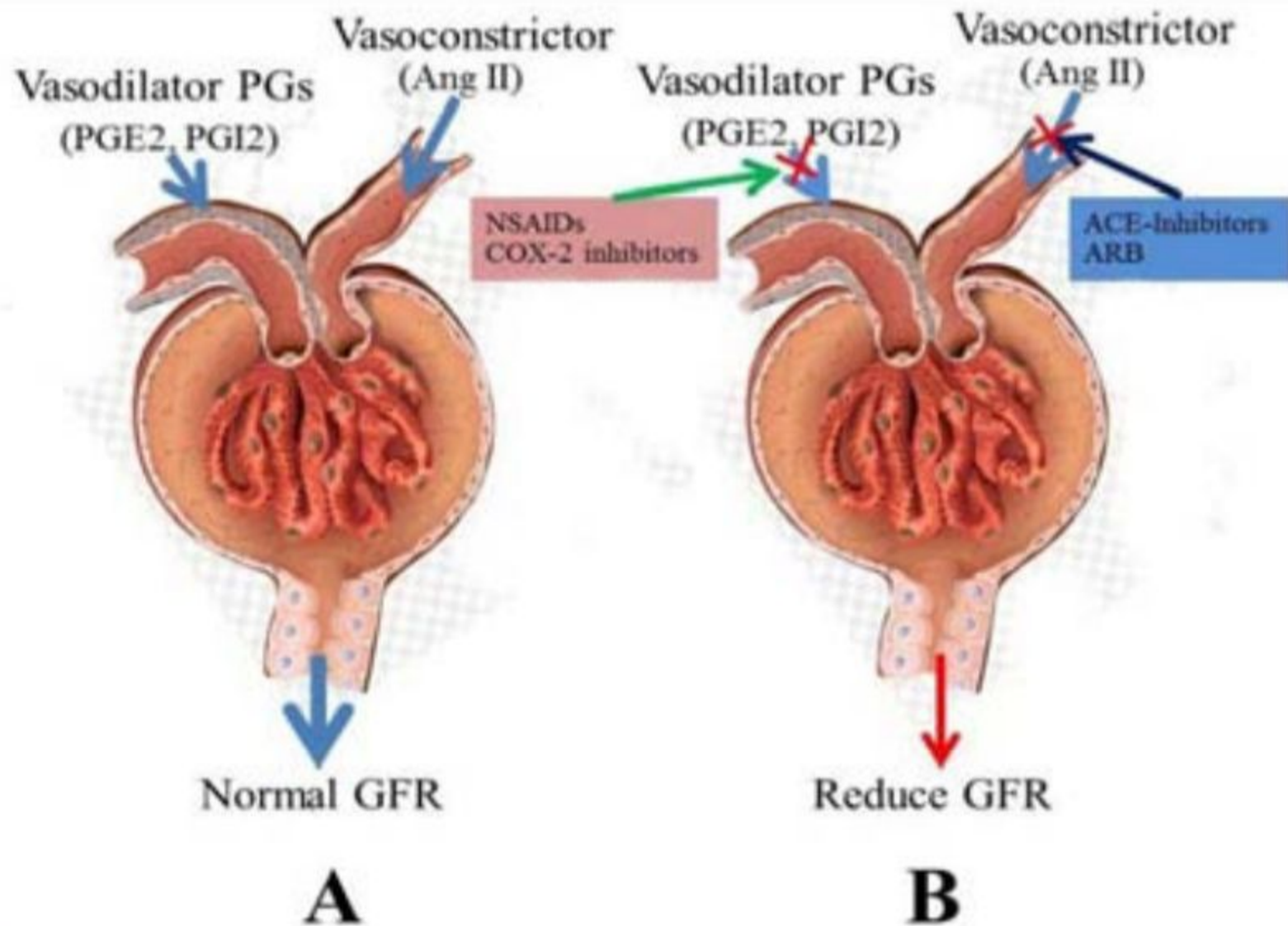


Figure 2: Regulation of renal blood flow & glomerular filtration in the kidney. PGE2 and PGI2 play an increasingly important role in maintaining renal perfusion by causing enhanced pre-glomerular vasodilation and angiotensin II (Ang II) produce efferent arteriole vasoconstriction to maintain normal GFR (A). Treatment by NSAIDs and COX-2 inhibitors can adversely affect renal function by blocking the production of autoregulatory prostaglandins resulting in a decline in GFR and treatment with ACE inhibitors or ARB can also further reduce glomerular perfusion and contribute to renal failure (B).

Renal syndromes associated with NSAID use

Acute kidney injury (hemodynamically-mediated or acute tubular necrosis)
Acute interstitial nephritis
Nephrotic syndrome (minimal change disease or membranous nephropathy)
Hyponatremia
Hyperkalemia/type 4 renal tubular acidosis
Hypertension/edema
Acute papillary necrosis
Chronic tubulointerstitial nephritis/analgesic nephropathy
Uroepithelial malignancy

Source: Clive DM, Stoff JS. Renal syndromes associated with nonsteroidal antiinflammatory drugs. *N Engl J Med* 1984; 310:563.

Graphic 90018 Version 1.0

مبارح بلشنا بال NSAIDs induce AKI ...

وعرفنا انه في تسع ميكانزمات لل NSAIDs renal syndrome

واخذنا اول نوع ... Functional mediated AKI

اللي كان باختصار ، انه ال NSAIDs بما انها بتمنع ال PGs بالتالي رح يصير V.C لل Renal aretry ... ويقل ال GFR ... ويتراكم ال srcr

وعرفنا انه ال PGs دورها الاساسي هو ال Dilatory effect

ولكن في حالات معينه ٤ بيكون في Effect اضافيه لل PGs

غير ال V.D

واتفقتنا انه هاي ال Effect

1□promot Secretion of Renin

2□Impair Na reabsorption in henle loope and collicting duct

3□Partially Antagonise the ADH

وهادي ال Effects بتكون بحالات ال Hypotension وال

□ Activation of Ang2 , Vasopressin , Norepinephrine

و هاي ال Effect هي اللي رح تكون مسببه لل Electrolyte changes

ف رح نشوف تكمله لل NSAIDs Renal Syndrom المتعلقه بال

Electrolyte Disturbance ...

1□HyperKalemia

2□hyponatremia

3□Edema /Hypertension

ناخذ وحده وحده ٤٤

1□Hyper K

بال Condition اللي قولناها ال PGs Effect رح يتثبط بال NSAIDs

وبالتالي رح يقل افراز ال Renin , ورح يقل ال Aldosterone

ورح يزيد ال ADH effect

لما يقل ال Renin فالمسار التالي رح يتثبط ٤

Renin → Ang1 → Ang2 → Aldosterone

ومن المعروف انه ال Aldosterone وظيفته بال Distal tubule

ب يرجع فيه وملح (Na/H₂O) للجسم وبيرمي بدالهم ال +K

فلما ال Aldosterone يتثبط ٤٤ رح يتراكم ال +K + ويصير عنا

+Hyper K

طبيب هل معنى الكلام انه اي مريض رح ياخذ NSAIDs رح يصير عنده ارتفاع بالبوتاسيوم ؟؟؟ ؟؟

Normal K^+ level $\Rightarrow 3.5 - 5.3 \text{ Meq/L}$

عشان يعرفو هل ارتفاع ال K^+ رح يكون mild ولا Sever
راحو عملو تجربه ع 50 مريض ماشيين ع Indomethacin
وراقبو ال K^+ Level وخلال Few day لاحظو القيم التاليه :

40% من المرضى ارتفع البوتاسيوم عندهم بنسبه 0.5 Meq/L

و 34% منهم ارتفع ال K^+ بنسبه $0.5 - 0.9 \text{ Meq/L}$

و 26% ارتفع ال K^+ ل 1 Meq/L او اعلى من 1

فالنتيجه انه اغلب المرضى كان عندهم +Mild Elevation in K

اما اللي بنخاف يصير عندهم Moderate - Sever hyperKalemia
الحالتين التاليتين ؟؟

1 NSAIDs induce low GFR

يعني مريض ماشي ع NSAIDs وصار عنده

Functional AKI

وقل ال GFR

لما يقل ال GFR بتقل كميته ال $\text{Na/H}_2\text{O}$ الواصلين لل Tubule اللي كان من المفروض انه ال Tubule يرجع الميه وال Na
ويرمي بدالهم K

فالنتيجه رح يقل ال K excretion ويتراكم ال K^+ بالدم ...

2 pateint take Drugs that Rise K^+ level

.... As ACEIs ,ARBs , K^+ sparing Diuretic

هيك خلصنا ال HyperK

هيك خلصنا ال HyperK

نشوف ثاني Electrolyte Disturbance

2 NSAIDs may induce hyponatremia

ال NSAIDs بتزود ال ADH effect

ف ال ADH بيقلل اخراج ال H_2O بس وما اله تاثير ع ال Na فبيحبس الميه بالجسم فبتزيد كميته ال H_2O بالدم مقارنة بال Na

When NSAIDs may worsen the Hyponatremia ??

1-In pateint with SIADH

المرضى اللى عندهم ال SIADH بيكون ال ADH بينفرز زياده عن اللزوم ويبرجع ميه للجسم بزياده بدون Na

لانه ال Diuretic بتمنع ال Na reabsorption بالتالي لو ال NSAIDs اثرع ال Na في مريض اصلا بياخذ Thiazide ممكن ال HypoNa will be Worse

فإن NSAIDs بتثبط هاد ال Effect وبالتالي رح يزيد امتصاص ال Na ويصير Na Retention

B lactam antibiotic especially pencillin and cephalosporin ●1□

خلال اسبوع او اسبوعين من اخذ ال B lactam وغالبا بيكون مصحوب ب Rash و Fever و eosinophilia

2 • NSAIDs

اما ال NSAIDs عشان تعمل AIN بيكون بعد استخدامهم لمدة 6 شهور

وشفنا بالبوسنات السابقة ان ال NSAIDs بتعمل Functional AKI

خلال Days من استخدامهم

اما بال AIN بيكون استخدام ال NSAIDs لمدة لا تقل عن 6 شهور ..

Antimicrobial sulfonamides, including trimethoprim-sulfamethoxazole●3□

4●Ciprofloxacin and, perhaps to a lesser degree, other quinolones

5 Diuretics, including loop diuretics such as furosemide and bumetanide, and thiazide-type diuretics

67●Cimetidine (only rare cases have been described with other H-2 blockers such as ranitidine)

7●Allopurinol

8●Proton pump inhibitors (PPIs) such as omeprazole and lansoprazole

97●Indinavir

- 5-aminosalicylates (eg, mesalamine)

111●Anticancer drugs, such as immune checkpoint inhibitors (ICPi; such as ipilimumab and ..(nivolumab

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

ال AIN ما بتعتمد ع ال Drug dose يعني ممكن تحصل عند جرعه قليله او عند جرعه عاليه فهو Dose independence

□recurrence or exacerbation of AIN can occur with a second exposure to the same or a related drug

يعني فرضا مريض اخذ Pencillin G وصار عنده AIN ..

ف ممكن لو اخده كمان مره تتكرر عنده ال AIN

أو ممكن related drug یعنی، مريض صار عنده AIN من البنسيلين

ف وار د خدا لو ا خ د Cephalosporin بر دو ی ص یر ع نده AIN

لأنه الدوائين ... Structurally Related

□patients who develop AIN secondary to a cephalosporin should avoid other cephalosporins or □.(penicillins

ال Onset لى Drug induce AIN

(several weeks, to many months (as occurs following a first exposure to an offending drug

Exposure من أسابيع لشهور من اول

ما عدا ال Rifampin من أول يوم بأول Exposure ممكن يصير AIN

- from three to five days (as occurs with a second exposure to an offending drug)

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

□Clinical manifestations — With AIN from any cause, patients may present with nonspecific signs and symptoms of acute kidney dysfunction. These may include the acute or subacute onset of nausea, vomiting, and malaise. However, many patients are asymptomatic . Patients may be oliguric or nonoliguric

البوست القادم رح نشوف ال Ttt لل AIN

#لعلي_أفيدك ؟

Antibiotics	β -lactam drugs*
	Fluoroquinolones*
	Rifampin*
	Sulfa-based drugs*
	Vancomycin
	Minocycline
	Ethambutol
	Erythromycin
	Chloramphenicol
Antiviral medications	Acyclovir
	Abacavir
	Indinavir
	Atazanavir
GI medications	Proton pump inhibitors*
	Histamine-2 receptor blockers
Analgesics	Nonsteroidal anti-inflammatory drugs*
	Selective COX-2 inhibitors
Anti-seizure drugs	Phenobarbital
	Phenytoin*
	Carbamazepine
Other drugs	Allopurinol*
	5-Aminosalicylates*
	Captopril
	Interferon
	Cyclosporine
	Anti-angiogenesis drugs (tyrosine kinase inhibitors)
	Diuretics

*Most common offending agents.

Acute Interstitial Nephritis causing drugs

www.medinaz.com

Sulfonamides

Methicillin

Ampicillin

Rifampicin

Thiazides

NSAIDs

Allopurinol

Cimetidine

“SMART Nephrons
Are Crying”



Management of suspected acute interstitial nephritis



AIN: acute interstitial nephritis; IV: intravenous.

* The clinical presentation of AIN includes acute kidney injury and sterile pyuria, possibly associated with rash and eosinophilia; the duration between initiation of an offending agent and onset of acute kidney injury is variable. Refer to UpToDate topics on diagnosis of AIN for details.

¶ Many drugs can be associated with AIN. In selected situations in which multiple potential offending agents are being used, they may be discontinued sequentially rather than consecutively, depending upon the availability of alternatives. For instance, if one potentially offending agent is considered crucial and has limited alternatives, the other drug may be discontinued first and the more crucial drug discontinued only if there is no improvement. Refer to UpToDate topics on etiology of AIN for details.

Δ Refer to UpToDate topics on contraindications to kidney biopsy for details.

◇ Some, but not all, authors of the related topic (refer to UpToDate topics on the treatment of AIN for details) recommend IV methylprednisolone (eg, 500 to 1000 mg daily) as initial treatment for 3 days followed by oral prednisone if renal replacement therapy is imminent. If renal replacement therapy is not imminent, we initiate oral prednisone (typically 1 mg/kg/day).

§ Glucocorticoids may be started after the biopsy, if the biopsy is able to be performed on the same day. In all other cases, empiric initiation of glucocorticoid therapy is reasonable prior to the kidney biopsy.

¥ Some patients may not fully recover to their preinjury baseline. Recurrence of acute kidney injury while tapering glucocorticoids should trigger an evaluation for alternate etiologies. Refer to UpToDate topics on management of AIN for details.

بدأنا مبارح بال (Acute Intersitial nephritis (AIN

وشفنا ال Drug that induce AIN واشهر مجموعتين هي ال
.. B lactam & NSAIDs

اليوم ان شاء الله رح نشوف ال Managment لل AIN ..

وهاد Algorithim ملخص لل ↓ Managment Step

📄 https://t.me/l3lee_afeedk/439

نبدأ مع ال AIN management ♀♀

اول شي بنعمله هو ايقاف الادويه المسببه لل ↓ AIN ...

📄 Discontinue the offending Drug that cause AIN
...Discontinuation of the potential causative agent is a mainstay of therapy

في عنا ثلاث recommendation لتوقيف الادويه المسببه AIN

1📄●We discontinue the potentially offending drug in nearly all patients with suspected AIN.

2📄●If there are multiple potentially offending drugs, we generally discontinue them sequentially if the acute kidney injury (AKI) is mild; however, we discontinue them simultaneously if the AKI is severe.

3📄● we do not discontinue the potentially offending drug if the drug is a crucial treatment for a severe disease process, there are no reasonable alternatives, and the diagnosis is uncertain (eg, a kidney biopsy has not been performed).

📄يبقى اول خطوه بنوقف ال offending drug

تاني شي بنقيم حالة المريض

📄 Assess the severity

المريض رح يكون جاي ب AKI و Suspected يكون AIN ...
في عنا احتمالين لحالة المريض .

1📄Sever AKI and need dialysis within 24-72hr

2📄Not severe AKI and no need for Dialysis

بدون ما ياخذ IV

2- لو نتيجة ال Biopsy كانت بالفعل AIN والمريض ما استجاب ع العلاج فمممكن يكون المريض عنده substantial chronic kidney damage rather than acute inflammatory injury فالمرضى اللي عنده Sever chronic changes وما فى اى Evidence لل

acute inflammatory infiltrate

فهاد المريض ما رح يستجيب ع ال Prednison فبنقل الجرعه بالتدريج وبنوقف ال Prednison

3- لو ال Biopsy أكدت وجود

,inflammatory infiltrate composed of T cells, plasma cells, and eosinophils in the interstitium

ساعتها عنا خيارين

□

اما نطول مده العلاج بال prednison ل 8-12 week

□

او بنشفت المريض ع (MMF mycophenolate mofetil) لو عنده ما يمنع الاستمرار ع Glucocorticosteroid

□□□□□□□□□□□□□□□□

Patients who fail to respond to initial therapy

In pateint with biopsy-proven AIN and documented failure to respond to or withdraw from glucocorticoid therapy

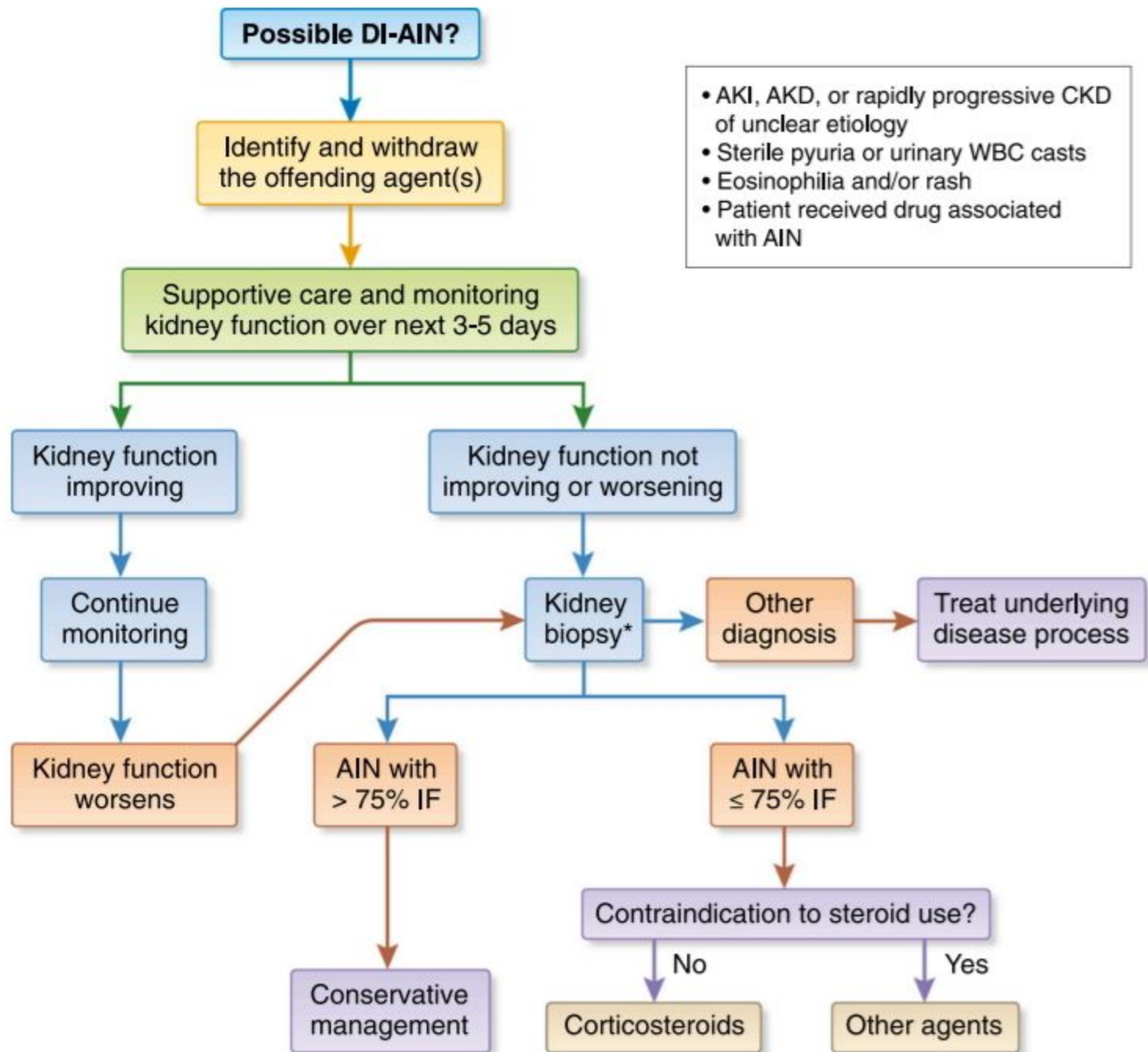
Start with mycophenolate mofetil (MMF)

started at a dose of 1 g daily in divided doses and titrated up to a dose of 2 g daily, if tolerated.

In Pateint who fail withdraw from glucocorticoid therapy after six months the addition of MMF, most patients were able to discontinue glucocorticoids ... And improve serum creatinine

وهيك بنكون خلصنا ال AIN management □□

#لعلي_أفيدك ؟



There is no definitive evidence that corticosteroid therapy is beneficial in NSAIDs AIN
. However, a course of prednisone may be considered in patients whose kidney failure persists more than one to two weeks after the NSAID has been discontinued

كيف ال Aminoglycoside (AMG) بتعمل ATN ...

ومين الناس المعرضه لل AMG toxicity

♀#Drug_Induce_ATN

مجموعه ال AMG اللي بتتضمن

Amikacin ,Gentamycin ,Streptomycin ,Tobramycin ,
Neomycin

من أشهر المضادات الحيويه اللي بتشتغل ع Gram - bacteria
عبر تثبيط ال 30S subunit وبالتالي بيمنع تكوين بروتينات البكتريا

ال AMG لما توصل لل glomerulus بتتفلتر وبتعدي ع ال Tubule ..

ال (Phospholipid(PL Proximal Tubule عليه negative charge -

وال AMG فيه مجموعه Amine بتتأين بشحنه + داخل الدم

فال AMG بشحنته ال + وهو معدي بال Proximal Tubule

بيروح يشبك بال PL ابو شحنه سالبه ..

وبيرتبطو ببعض وبيروحو يرتبطو ببروتين اسمه megalin

هاد ال Megalin عباره عن

... KD cell surface Receptor has a high affinity to protein with positive charge aminoacid 600

بعد ما ال AMG يرتبط بال Megalin بيدخل لداخل ال Proximal tubule تحديدا اول جزئين من ال Proximal Tubule
S1&S2

وبالتالي بيتراكم ال AMG داخل ال S1,S2 tubule وال Distal tubule

وبيعمل Damage لل Tubular cell

ال megalin بيتواجد بال Proximal tubule وال Glomerulus podocyte وال Inner ear

عشان هيك هدول الاماكن عندهم Affinity عاليه لتراكم ال AMG

□□□□□□□□□□□□□□□□

لو مريض مشى ع أحد أدويه ال AMG متى بيزيد ال Risk عنده لل nephrotoxicity ولو صارت متى بيبين ارتفاع ال SrCr
..□

Serum creat rise 5-7 day of AMG therapy

يعني بعد 5-7 ايام من ال AMG بيبدا ال SrCr يرتفع وفي بعض المراجع بتقول من 6-10 ايام ..

وباحتاج المريض 21 يوم من بعد ايقاف الدواء ليرجع ال Srcr للطبيعي الا لو كان المريض Septic او عنده hypovolemia
فباحتاج وقت اطول ليصير Tubular Recovery

في عنا بعض ال Risk Factor اللي بتدخل المريض ب
AMG nephrotoxicity

1●Prolonged duration of therapy

كل ما زادت مده العلاج ،ببزيدي فرصه تراكم ال AMG بال Tubule وببزيدي ال Tubular damage ويمكن يوصل المريض ل Irreversible kidney damage even in Low doses

2●Advanced age

مل ما كان المريض اكبر سنا ،كل ما قلت كفاءه ال Tubule لل Repair وال Regeneration لل Damaged Cell

3●Comorbid disease

CKD ,DM ,leukemia Increases risk of AMG AKI

4● Reduced effective arterial volume

لو ال GFR اللي بيوصل للكلية قليل ففرصه ال Cell Ischemia وال Damage بتزيد

Sepsis●5□

ال Toxin بال Sepsis بتعمل Kideny damage فبتعزز ال AMG nephrotoxicity

6 Concomitant medications

لما يكون المريض ماضي ع اكثر من دوا nephrotoxic فيزيد ال
Tubular cell damage

من الادويه اللي اعطائها مع ال AMG بيزود ال Toxicity↓

Implicated medications include furosemide, (NSAIDs), angiotensin-converting enzyme inhibitors, cisplatin, cyclosporine, clindamycin, and vancomycin

7●Elevated plasma drug concentrations

.Careful monitoring of plasma levels is an important component of aminoglycoside therapy

المريض اللي ماشى ع Multiple dose يعني مثلا ماشى ع Gentamycin كل 8 ساعات

لو قسنا ال Peak level لل Gentamycin او ال Tobramycin

وكان اكثر من 10mcg/ml بهلحاله بتزيد ال nephrotoxicity

فالمريض اللى بياخد Multiple dose يفضل نقيسله بعد كل جرعه بياخدها ال Peak level

وينقاسله قبل كل جرعه ال Trough level

ال Trough level ببين قديش ضايل تركيز من الدوا قبل ما نعطي الجرعه الثانيه
يعني لو مريض اخذ gentamycin اول جرعه الساعة 12 am
والمفترض الجرعه الثانيه تكون 8am ..

بعد نص ساعه من جرعه ال 12 لو سحبنا عينه وقسنا تركيز ال Gentamycin بنشوف تركيز ال Peak

اما لو سحبنا عينه قبل نص ساعه من جرعه الساعة 8 بنقدر نشوف ال Trough level

طيب لو المريض ماشي ع Once daily dose مثلا بياخذ
mg gentamycin once 240

فبنكتفي بال Tough level قبل كل جرعه

elevated trough levels (>2.5 mcg/mL) have been associated with nephrotoxicity in a once-daily
aminoglycoside dosing

8●●Type of aminoglycoside

ال nephrotoxicity لل AMG مبنية حسب قديش الدوا بيقدر يرتبط مع ال Phospholipd of Tubular cell ..

كل ما ارتبط الدوا اكثر، كل ما رح يتراكم بصورة اكبر داخل ال tubule cell ويعمل More Damage

gentamicin has the greatest nephrotoxic potential, followed in decreasing order of nephrotoxicity by
tobramycin, amikacin, and netilmicin

Gentamicin > Tobramycin > Amikacin

ال Amikacin اقل واحد بال toxicity وافضل واحد بال efficacy

9●●Frequency of dosing

اغلب الابحاث بينت انه ال Once daily dose أقل Toxicity من ال Multidose
patients with ascites, burns covering >20% of total body surface area, cystic fibrosis, end-stage
renal disease, endocarditis, infants, mycobacterial infections, or pregnancy

البوست القادم رح نشوف ال prevention of AMG nephrotoxic effect

#لعلي أفيدك ٤



Filtered
Aminoglycoside

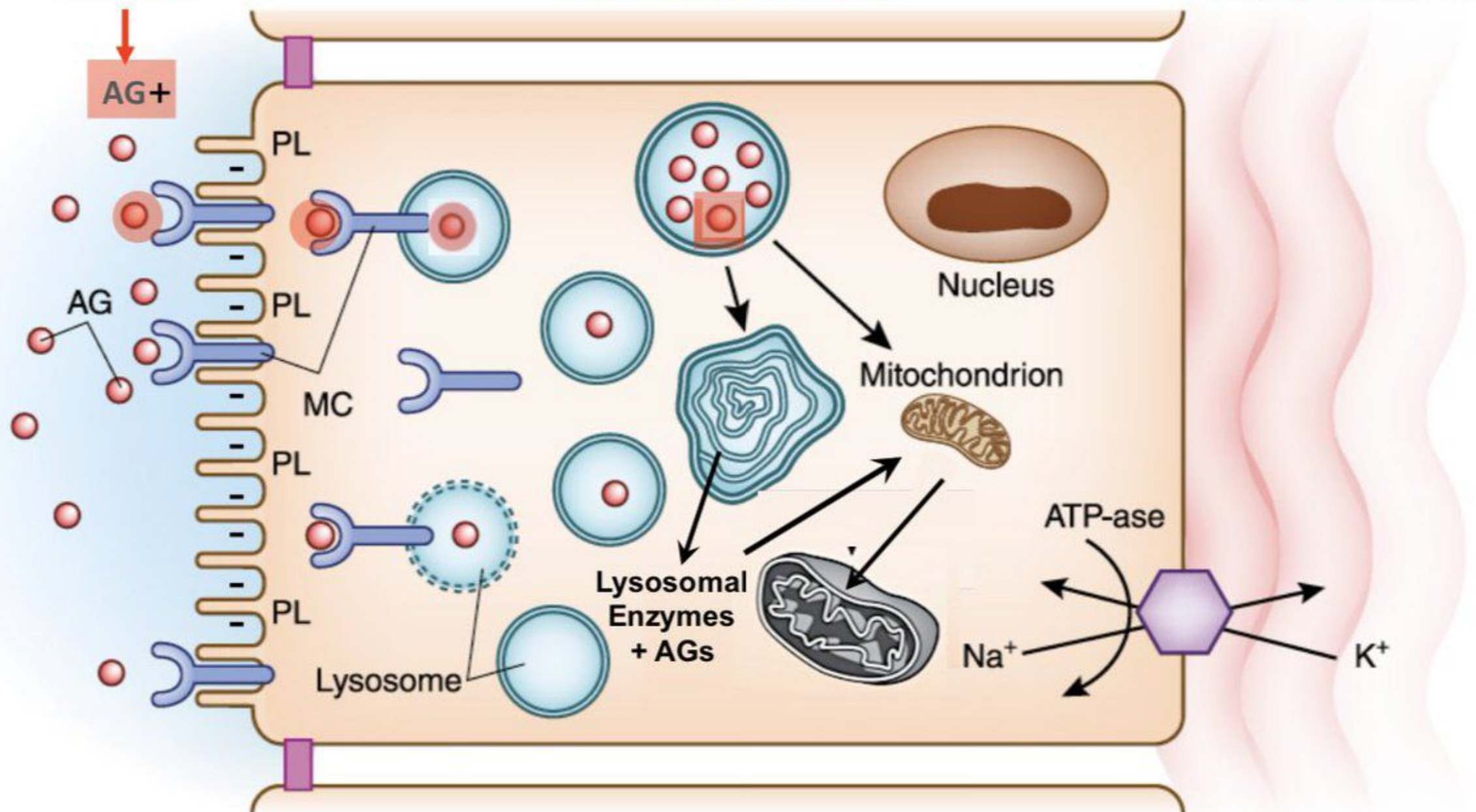
National Kidney Foundation*

Aminoglycosides Nephrotoxicity

APICAL

PROXIMAL TUBULE

BASOLATERAL



Proximal tubule cell transport and

charge — Multiple amine groups on the aminoglycoside molecule confer a cationic charge at physiologic pH [\[11,12\]](#). As a result, aminoglycoside molecules readily bind to anion phospholipids within the plasma membrane of the PTC in a saturable, electrostatic manner [\[11-14\]](#). The relative affinity of an aminoglycoside for the PTC plasma membrane correlates with the nephrotoxicity observed in clinical practice [\[4,15-17\]](#):

- [Neomycin](#), which has the highest affinity for the PTC binding site, has the greatest nephrotoxicity of the aminoglycosides.
- [Tobramycin](#) and [gentamicin](#) have lower binding affinity, conferring less nephrotoxicity.
- [Amikacin](#) has even less binding affinity and, likewise, has less nephrotoxic potential than [tobramycin](#) and [gentamicin](#).
- [Streptomycin](#), which has the least affinity for the PTC binding site, has the least nephrotoxicity [\[4,15,16\]](#).

تكلما المره الماضيه عن ال AMG (Aminoglycoside nephrotoxicity) ووصلنا لانه مجموعه ال AMG الها Affinity عاليه للارتباط بال Tubule cell والتراكم داخلها وبالتالي بتعمل Damage لل Cell

وعرفنا انه ال Gentamycin هو اكثرهم Toxic effect وال Amikacin أقلهم بال nephrotoxicity

وشفنا كمان انه ال Once daily dose افضل من ال Multiple dose ما لم يكن المريض عنده ما يمنع ال Once dose زي الحالات التاليه ٩:

once daily dose Not for use in patients with ascites, burns covering >20% of total body surface, area, cystic fibrosis, end-stage renal disease, endocarditis, infants, mycobacterial infections, or pregnancy

اليوم رح نكمل اخر جزء بال AMG nephrotoxicity ♀

شو هي ال Manifestation اللي بيجي فيها المريض :
1 Non oligurea AKI

2 Distal tubular dysfunction
لو ال AMG أثر ع ال Distal tubule ←← رح يفقد قدرته على تركيز ال Filtrate , وبالتالي رح تزيد كميته ال Urine

كمان ال Distal tubular dysfunction بتقلل ال ADH sensetivity ←← فالنتيجه ←← Polyurea

3 Electrolyte abnormalities — Hypomagnesemia, hypokalemia, hypocalcemia, and hypophosphatemia are infrequently observed. This is likely secondary to the decrement in proximal tubule transport that occurs during aminoglycoside-induced nephrotoxicity

اي مريض عنده Hypomagnesemia بتزيد عنده فرصه ال nephrotoxicity .. عشان هيك لازم تتزبط ال Electrolyte عند المريض قبل ليبدأ بال AMG ..

Prevention of aminoglycoside nephrotoxicity.

Prevention of aminoglycoside nephrotoxicity.

● Selection of the least toxic aminoglycoside, when possible as Amikacin

● Keep adequate hydration

(avoiding aminoglycosides in patients with reduced effective arterial volume (or optimizing volume status prior to giving aminoglycosides)

● Correcting hypokalemia and hypomagnesemia prior to administering an aminoglycoside.

● Pharmacokinetically monitoring aminoglycoside therapy and utilizing a once-daily dosing regimen in selected patients have also demonstrated benefit

● adjusting the dose for renal function

لو مريض عنده مشاكل بالكلى وكان مضطر يمشي ع AMG وما في خيار بديل ،، ساعتها بيمش المريض ع Renal dose حسب ال GFR

وهاد الملف فيه جرعات ال AMG حسب ال GFR

https://t.me/l3lee_feedk/177

● limiting the duration of therapy to 7 to 10 days

● minimizing concomitant nephrotoxic medications

● vitamin E, vitamin C, and selenium have been effective in preventing gentamicin nephrotoxicity

#لعلي_أفيدك ٤ مسا الخير ٤٤٤

مريض عمره 70 سنة صار عنده MI وعمل

.... Angiography with Radiographic contrast

كان داخل ب 2 mg/dl srcr وبعد 48 ساعه من ال Angiography ارتفع ال Srcr ل 2.5mg/dl

شو اللي صار مع المريض؟ ٤٤

Contrast-associated AKI (CA-AKI) "#"

Acute kidney injury (AKI) may develop after administration of iodinated contrast material

فال Radiographic Contrast Media تعتبر من ال Agent اللي بتعمل (ATN) Acute Tubular Necrosis ...

□□□□□□□□□□□□□□□□

في عنا ثلاث أنواع لل Contrast المستخدمه للتشخيص وبنصنفها حسب ال Osmolality تبعها :

Blood osmolality :290mosmol/kg □□□□

(1□ High Osmolal Contrast: (1400-1800 mosmol/kg

ال High osmolal اول جيل تم اكتشافه من ال Contrast

وهو اكثر نوع بيعمل Nephrotoxic Effect عشان هيك بطلو يستخدموها

(2□ Low Osmolal Contrast : (500 to 850 mosmol/kg

أقل Nephrotoxic effect من الجيل الأول ...

low-osmolal agents include the nonionic agents (iohexol, ioversol and iopamidol) and the ionic agent, ioxaglate

3 Iso-osmolal agents
(iso-osmolal with plasma (290 mosmol/kg

ال Iso osmolal أفضل نوع وأقلهم من حيث ال Nephrotoxic effect .. لأنها ال Osmolality نفس ال blood

Only one iso-osmolal agent (iodixanol) is available..

Lower doses (<125 mL) of contrast tend to be safer

كيف ال Radiographic contrast بتعمل ATN :

في أكثر من ميكانيزم لل (CA-AKI :

: Contrast induce ATN

ال Contrast بتعمل Direct cytotoxic effect عبر Free radical

contrast induce Renal Ischemia

بما انه ال Contrast ال High او ال Low الهم Osmolality اعلى من ال Blood osmolality فبتسحب الميه من الجسم

وبتعمل

.. Osmotic Diuresis

فبتقل كميه ال Circulatory volume ..

عشان هيك ال IsoOsmolal أفضلهم لأنها ما بتعمل Diuresis

ووجدوا ان ال contrast بتعمل Renal V.C عبر تثبيط ال NO وتحفيز ال Endothiline وال Adenosine

وبالتالي بيقل ال GFR

وع الاغلب ال AKI الناتج من ال Contrast بنعتبره Functional AKI وقليل ليعمل Necrosis عشان هيك ال CA-AKI تعتبر

Reversible ويصيرلها Rapid Recovery خلال Few day

طبيب شو ال Presentation اللي بيجي فيها مريض ال CA-AKI

1 Mild increas in SrCr 24-48 after the procedure

Usually recover to normal within 3-7 day

2 Non oligurea in most pateint

المريض اول ما بياخد Contrast بصير عنده Osmotic diuresis

3 Oligurea in pateint with Moderate -sever CKD or in pateint with other causes of AKI ...

البوست القادم رح نشوف ان شاء الله ال Risk factor وال Prevention لل CA-AKI

#لعلي أفيدك



Renal Vasoconstriction

Imbalance of renal vasodilators and vasoconstrictors.

Increase in viscosity and reduction in medullary blood flow

Medullary hypoxemia --> Ischemia --> tubular necrosis



Treatment:

- Hydration
- NAC
- Fenoldopam

Cytotoxic effects of CM

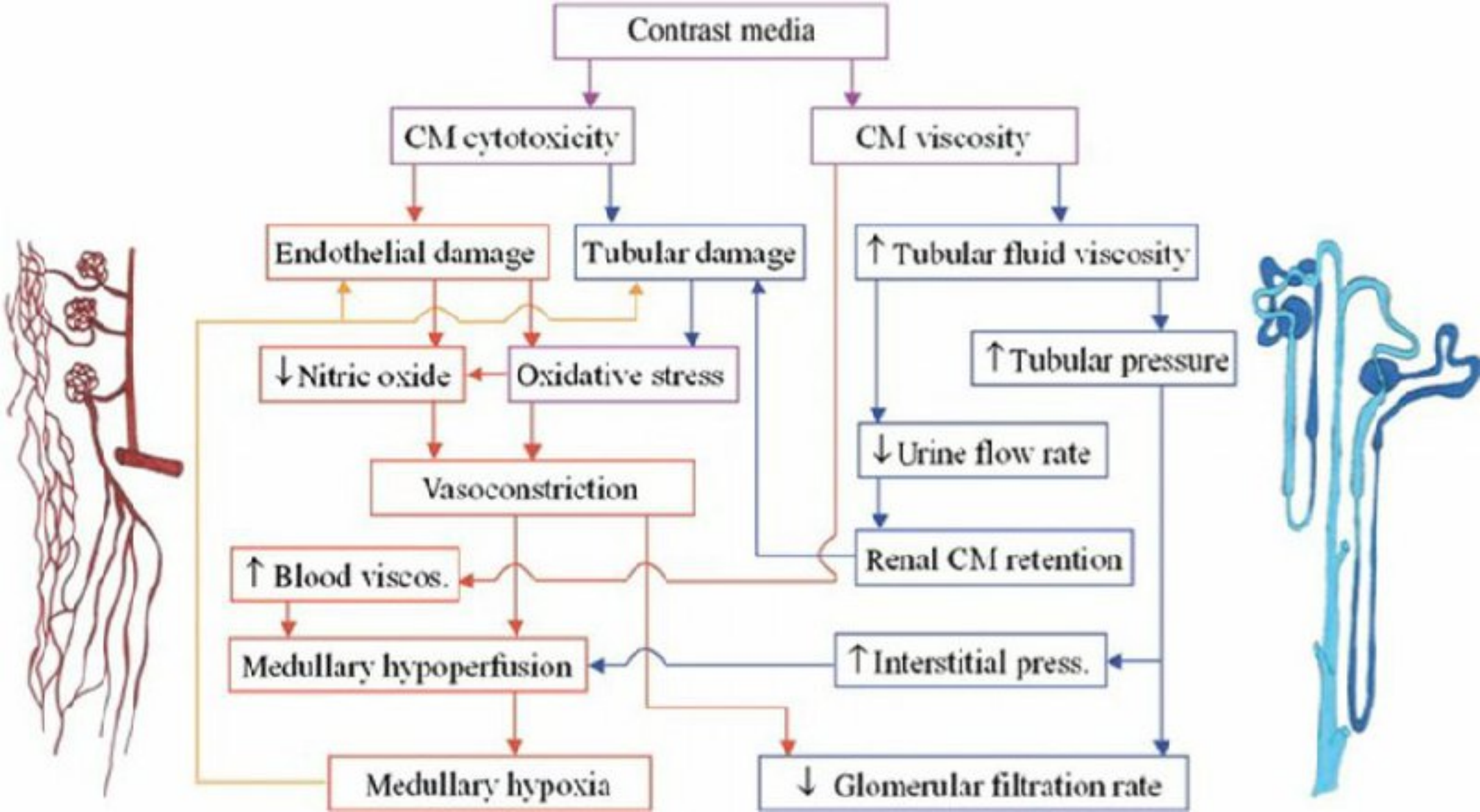
Generation of reactive oxygen species

Apoptosis of renal cells.



Treatment:

- NAC
- Sodium Bicarbonate

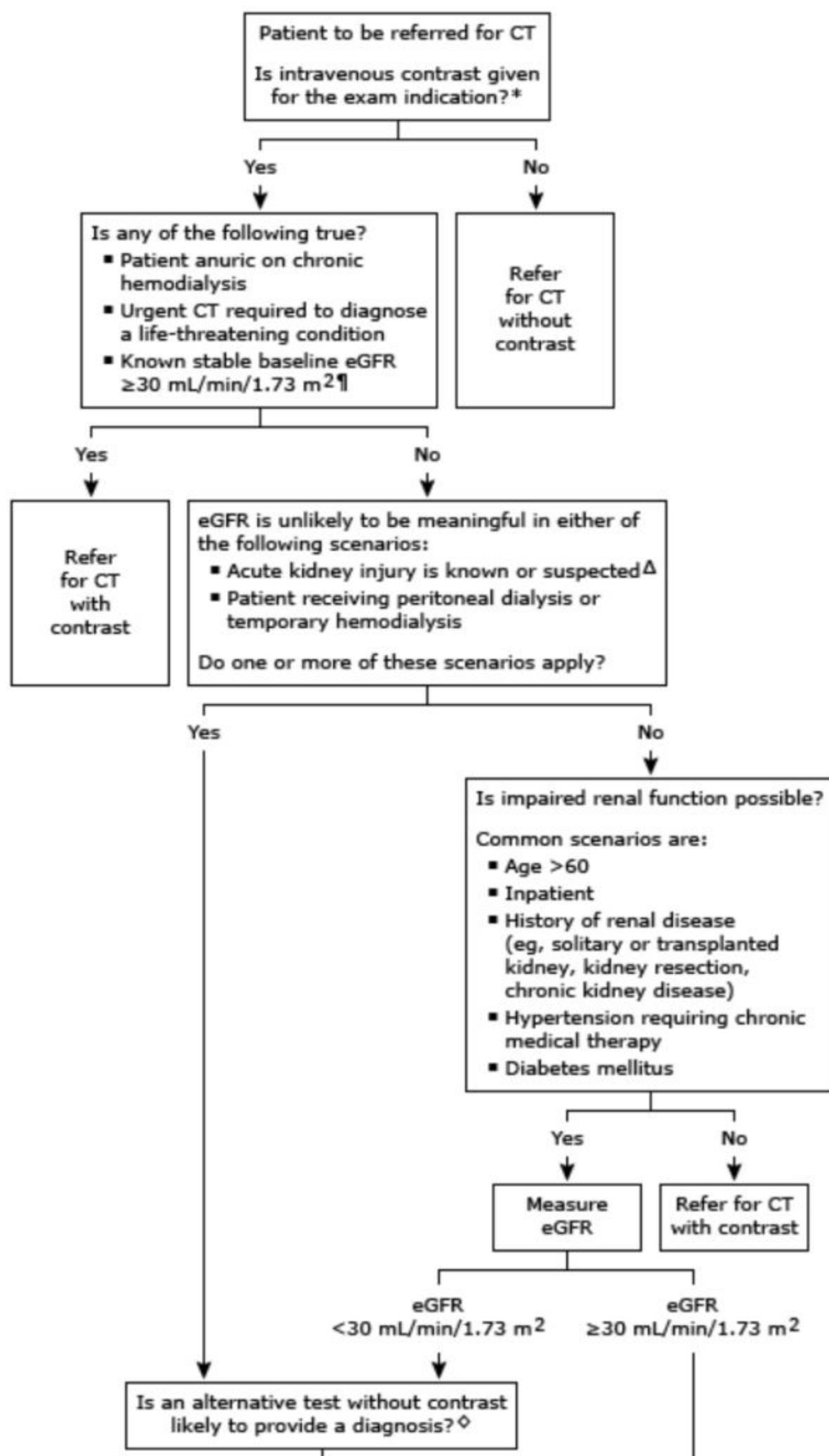




Graphic

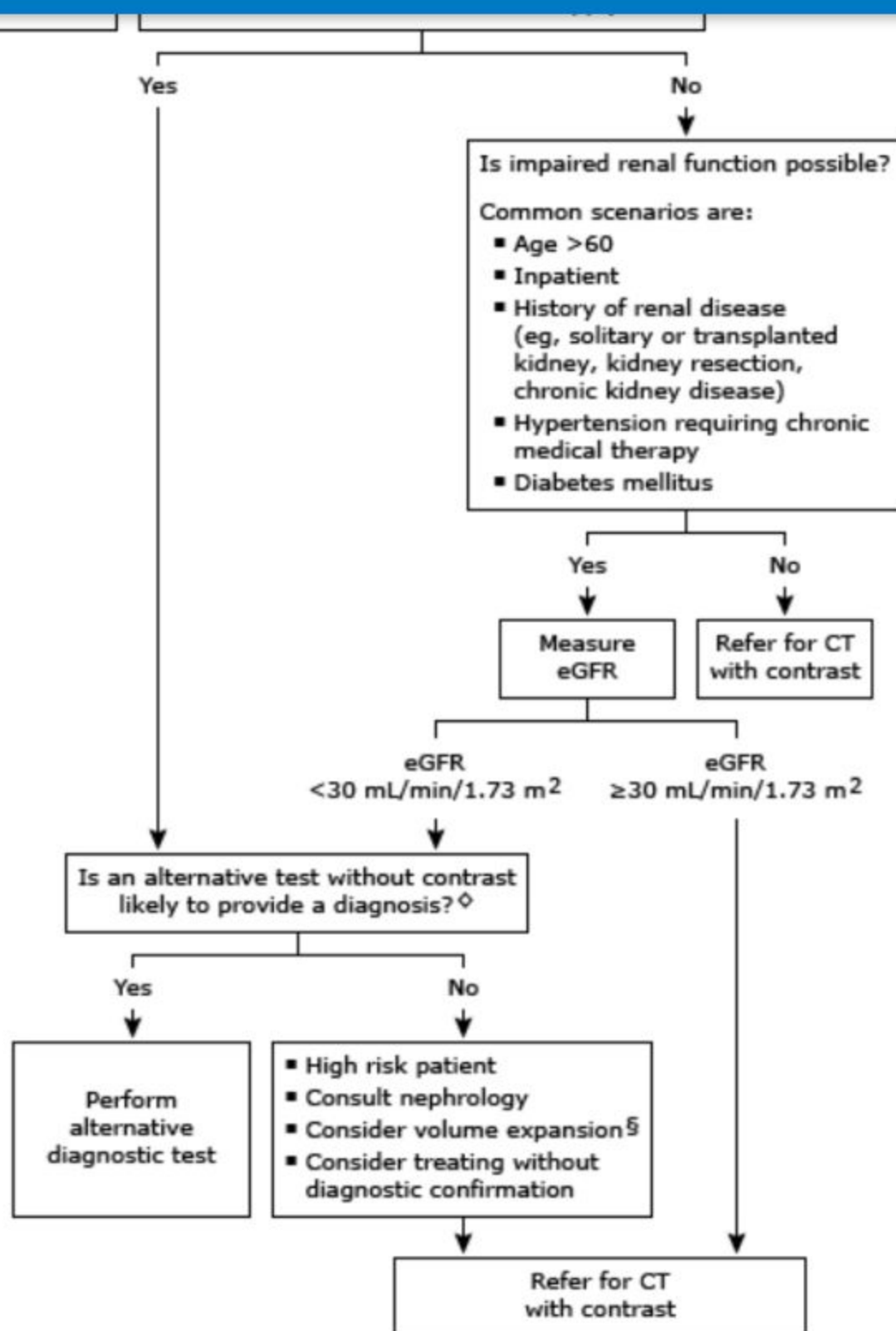


Patient evaluation for contrast administration for computed tomography: Concern for contrast induced nephropathy





Graphic



Standards for patient preparation and indications for contrast vary somewhat with each practice. Provider should refer to institutional policies for detailed guidelines in patients likely to require an intervention.

CT: computed tomography; eGFR: estimated glomerular filtration rate.

* Refer to UpToDate topics or the American College of Radiology (ACR) Appropriateness Criteria for CT contrast recommendations based on a specific exam indication. Enteric (oral or rectal) contrast is not associated with renal injury.

¶ Medical judgment should be used to determine whether baseline renal function is likely stable. In general, eGFR within 30 days in an outpatient and two days in an inpatient is likely to reflect baseline renal function if the medical condition and treatments have not been changing in the interim.

Δ Examples are patients with sepsis, myocardial infarction, or large volume hemorrhage.

متى نلجأ لعمل Assessment للـ GFR لمريض بده يعمل CT ومتى ما بنحتاج نقيم الـ GFR ومتى بحكي انه المريض محتاج اعمله وقايه من الـ AKI قبل ما ياخذ الـ Contrast

1- اول شي مين هم المرضى الي لازم نشوفلهم الـ GFR قبل الـ CT

1- Patient with history of kidney Disease

2- Patient with Hypertension and take Chronic medication

3- DM patient

4- Patient >60 year old (Optional)

2- اما المرضى اللي الـ GFR ما رح يفيدني بتقييم حاله الكلية:

1- Patient anuric with chronic hemodialysis

2- Patient undergo an Episode of AKI

مثلا Sepsis او ماشي ع Nephrotoxic drug او اي سبب عامل AKI
هنا الـ GFR مش حيكون ثابت وما رح يعطيني فكره عن حاله الكلية

3- Urgent life threatening condition need urgent CT

مريض من المرضى اللي ما بيلزمهم prevention therapy قبل الـ CT

1- لو كان المريض عنده الـ GFR اكبر من او يساوي 30 ف هنا المريض ما بيحتاج prevention

2- لو كانت حاله المريض Urgent ف ما بياخذ Prevention

3- لو كان المريض Anuric و ماشي ع Chronic hemodialysis

هنا الكلية بالاصل مش شغالة وما بتطلع Urine فما رح يفيد الـ Prevention

مريض من المرضى اللي بيحتاجو Prevention Therapy قبل الـ CT .. واللي بنعتبرهم High Risk patient to CA-AKI

1- لو الـ GFR اقل من 30ml/min

2- مريض عنده AKI لأي سبب كان وبده يعمل CT بنعطيه prevention therapy لمنع المزيد من الـ AKI

3- لو مريض اضطر يغسل Temporary hemodialysis وهو بالاصل مش مريض غسيل كلّي مزمن

او لو مريض بيغسل Peritoneal بهلالتين بيحتاجو Prevention

High risk pateint ك Multiple Risk factor والمريض عنده GFR 33-44 ml/min ال كان لو 4444 ويبيعطوهم Prevention Therapy

High risk pateint لل Prevention بنعمل كيف نشوف رح نشوف كيف بنعمل Prevention لل High risk pateint

#لعلي_أفيدك 4

Risk Factors for CIN

Patient-related Risk Factors

- Renal insufficiency
- Diabetes mellitus with renal insufficiency
- Age > 70 years
- Volume depletion
- Hypotension
- Low cardiac output
- Class IV CHF
- Other nephrotoxins
- Renal transplant
- Hypoalbuminemia (<35 g/l)

Procedure-related Risk Factors

- Multiple contrast media injection within 72 hrs
- Intra-arterial injection site
- High volume of contrast media
- High osmolality of contrast media

Table 1: Risk Factors for Contrast-induced Acute Kidney Injury

Fixed Risk Factors	Modifiable Risk Factors
Chronic kidney disease	Hypotension
Diabetes mellitus	Anaemia
Congestive heart failure	Nephrotoxic drugs
Age	Hypercholesterolaemia
Female sex	Periprocedural dehydration/ hypovolaemic states
	Pre procedural hyperglycaemia
	Contrast type and contrast volume

جمعہ مبارکہ ؟؟

مریض 60 سنه و DM ماشي ع Metformin وال eGFR عندہ 27ml/min ... ومحتاج CT with contrast ... كيف ممكن
نعمل Prevention لل
(CA-AKI (contrast associated Acure kidney Injury

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

شفنا اليوست السابق مين هم ال CA-AKI pt High risk
الى بيلزمهم Prevention قبل ال CT ولخصناهم كالتالى ٣٣٣ :

30ml/min GFR أقل من 30ml/min له

٢٠٢٤مریض عنده AKI لأي سبب كان وبده يعمل CT بنعطيه prevention therapy لمنع المزيد من الـ AKI

٣٩٤٣ لو مريض اضطر يغسل Temporary hemodialysis وهو بالاصل مش مريض غسيل كللى مزمن
او لو مريض بيغسل Peritoneal بهلحالتين يحتاجو Prevention

High risk pateint ك Multiple Risk factor عنده والمريض GFR 33-44 ml/min ال كان ال 4444ويعطوهم Prevention Therapy

□□□□□□□□□□

... Prevention Among High Risk pateint
.. CT Risk من اللى ذكرناها ومحتاج ل
كيف ممكن نمنع ال ... CA-AKI

1

لو في عنا Alternative test ويعطينا Reliable & Accurate Diagnosis زي مثلا
noncontrast CT, ultrasound, or magnetic resonance imaging
ساعتها بنلجأ لهم وما بنستخدم ال Contrast CT

1

لو ما في عنا خيار غير ال Contrast CT ساعتها بعمل للمريض

1 □ Volume expansion

2) choose the less nephrotoxic contrast (Iso-osmolal or low -Osmolal)

3 Withdrawal of metformin and nephrotoxic drugs in high-risk patients

□□□□□□□□□□

مين المريض الذي بنعمله .. Volume Expantion
المريض الذي Hypovolemia او Euvolemia بنعطيههم Saline كالتالي :
Inpatient or Outpatient

Some commonly used intravenous regimens for inpatients and emergency department patients include (time permitting):

● 3 mL/kg for one hour preprocedure, and 1.5 mL/kg/hour during and four to six hours post procedure (total postprocedure volume at least 6 mL/kg)

OR

●1 mL/kg/hour for 6 to 12 hours preprocedure, and 1 mL/kg/hour during and 6 to 12 hours postprocedure

Volume Expansion المرضي الذي Hypervolemia او الذي يبيغسلو ممنوع اعطائهم

- Infusion rates may need to be reduced in patients at risk for heart failure. (No benefit of bicarbonate infusion over normal saline)

□outpatients are sometimes given oral hydration, Some encourage patient-directed oral hydration .(before and after the scan (eg, total one to two liters

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

في حال المريض اللي رح يعمل CT وماشي ع metformin

حسب ال ACR guideline 2018

بنوقفله ال Metformin قبل ال CT ب 48 ساعه وبنرجعه بعد 48 hr من ال CT في حال وظائف الكلى كانت Normal اما لو صار AKI ما بنرجع ال Metformin الا لما ال Srcr يرجع للقيمه الطبيعيه

طیب لیش بنوقف ال Metformin مع انه مش Nephrotoxic □

لأنه من المتوقع انه لو ال Contrast عملت AKI ال GFR رح يقل وبالتالي ال Metformine clearance رح يقل

ويتراكم ال metformin بالدم ويعمل Lactic Acidosis ...

عشان هيك احتياطا بيتوقف ال metformin ويبرجع بعد 48 hr او بعد ما ترجع وظائف الكلى لقيمتها الطبيعيه ...

For patients who are not at high risk for AKI after contrast-enhanced CT, we do not prescribe prophylactic measures, do not withdraw nephrotoxic medications, and do not suspend metformin.

[illegible]

strong evidence : **في بعض ال Preventive method** **اللى ما عليها**

1 N-Acetylcysteine (NAC) -- glutathione Antioxidant and vasodilator. takes time, so it not in emergency cases.

According to UpToDate NAC is not used anymore ...

2□Ascorbic acid: Antioxidant , used immediately before.

Give oral ascorbic acid 3 g before procedure and 2 g twice daily for two doses after procedure. May have role in emergency cases

3□ Theophylline□ Fenoldopam □Prophylactic hemodialysis (HD) and hemofiltration: Do not use

وهيك بنكون خلصنا ال

Prevention of CA-AKI due to CT with Contrast

#لعلِّي أفيدك ؟

Table 2: Alternative non-iodinated contrast and non-contrast diagnostic imaging modalities.

Alternative Modalities	Indication	Limitations	Notes
Ultrasonography with color Doppler	Detection of gallstones, acute cholecystitis and biliary obstruction. Appendicitis in childrens. Hydronephrosis or ureteral stone. Acute or chronic pelvic pain in female such as ovarian cysts, hemorrhagic cysts, ovarian torsion, ectopic pregnancy and pelvic inflammatory disease. Solid vs cystic adenexal mass with evaluation of internal vascularity. Acute scrotal emergency in male such as testicular torsion or epididymo-orchitis. In unstable trauma patients, a FAST* scan can be used to assess for free fluid. Assessment of the extracranial carotid arteries for atherosclerotic disease. For evaluation of lower extremity DVT. Assessment of thyroid nodules.	Operator dependent	Non-ionizing, so useful in children and in women of child-bearing age, pregnancy. No intravascular contrast is required. Better than CT for gall stones detection, ovaian and testicular torsion, Soid vs cystic adenexal mass differentiation and assessment of thyroid nodules.
Carbon dioxide angiography	Infra-diaphragmatic intra-abdominal arteriography and interventions (renal, mesenteric, transplant organs, aortoiliac), Peripheral and central venography, IVC filters placement and retrieval, portovenogrpahy planning hemodialysis access and interventions, vascular malformation detection and intervention.	Avoided for coronary or cerebral angiogram, in patients with COPD, forms vapor lock if use along with nitrous oxide	Superior to ICM for detection of occult bleeding site, collateral circulation, arterio-venous shunting in tumors, for detection of reconstituted vessel distal to occlusion, visualization of portal splanchnic veins. Non-allergenic, non-nephrotoxic, inexpensive.
2D and 3D-TOF MR angiography	3D-Cerebral arteriography for stenosis, aneurysm and AVM or AVF. 2D and 3D-Cervical arteriography for stenosis, dissection and AVM or AVR Cerebral venography for dural venous sinus thrombosis.	Poorer resolution compared with conventional angiography, motion artifact	No contrast is required.
3D ECG-synchronized or peripheral pulse gated half-Fourier fast spin echo MR angiography	Evaluation of vessel morphology of peripheral MRA and MRV, Abdominal vessels including porto-venography	Susceptibility to field heterogeneity, Requirement of personnel having expertise in imaging, post-processing and interpretation.	No contrast is required, short acquisition time than Phase contrast and TOF MRA
Phase contrast MR imaging	Quantitative flow measurement in arteries of head, neck, thoracic and abdominal aorta. Assessment of pulmonary flows and pressure in pulmonary hypertension, congenital heart disease, renal artery stenosis.	Poorer resolution compared with conventional angiography, motion artifact, long acquisition time	No exposure to ionizing radiation, evaluation of blood flow and blood vessel morphology
SSFP MR imaging	Myocardial viability and function, Ischemic and non ischemic cardiomyopathy, congenital heart disease, coronary artery disease, renal artery stenosis	Requirement of dedicated personnel having expertise in cardiac imaging, post-processing and interpretation.	No exposure to ionizing radiation
Arterial spin labeling with/ without SSFP	Cerebral, renal and cardiac perfusion, Cerebral blood flow, Renal artery stenosis	Poor temporal resolution and spatial coverage, banding artifacts	No contrast is required, When combined with SSFP, it can be used as an angiographic imaging

Table 3: Preventive strategy to lower the risk of CIN as per EUR guideline 2011.

Parameters	Elective Procedure				Emergency Procedure
	eGFR>60ml/min	eGFR 45-60ml/min	eGFR 30-45ml/min	eGFR<30ml/min	
Metformin Use Per ESUR Guideline 2011					
When to stop	Continue	Intravenous contrast: continue Intraarterial contrast: stop 48hrs prior to exposure	Stop 48hrs prior to exposure	Metformin not recommended	Stopped at time of exposure
When to restart	Continue	Intravenous contrast: continue Intraarterial contrast: 48hrs after exposure	After 48hrs restart, if renal function at baseline		After procedure, monitor for sign of lactic acidosis. Restart 48hrs after exposure if renal function at baseline
Prophylactic Strategy Per EUR Guideline					
Intravenous (IV) contrast	None	None	IV or oral hydration	IV hydration	If risk factors, 300-500ml IV hydration
Intra-arterial (IA) contrast	None	Hydration	IV hydration	IV hydration	

Patients who are high-risk for contrast-induced nephropathy should have metformin withheld for a minimum of 48 hours and until the renal function has been shown to be normal

Important for me

Less important

The correct option of those given is to hold metformin for a minimum of 48 hours after the scan. This should be done for all patients who are at high risk for contrast-induced nephropathy. This patient is at high risk due to his age, history of chronic kidney disease and dehydration. It should continue to be held until renal function has returned to the patient's baseline.

لو مريض Cancer وماشي ع Cisplatin وبعد 5 ايام من العلاج ارتفع عنده ال SrCr وصار عندHypomagnesiumia
هاد معناته انه صار معه AKI بسبب ال Cisplatin

يبقى لو كان ال Pateint presentation بعد ال Cisplatin
هو ارتفاع في ال SrCr وانخفاض في ال Mg level وممكن Salt Wasting يعني يجي المريض ب
polyuria, hypovolemia, and hyponatremia

معناته

Cisplatin_Induce_Nephrotoxicity#

ف ال cisplatin يعتبره من الادويه اللي إلها ..
Dose Limiting Nephrotoxicity

وفي اكثر من ميكازم بتخلي ال Cisplatin يعمل AKI ..

1 Tubular cell Injury وبالتالي Renal Cell death
عبر تكوين FreeRadical

2 بتعمل Injury لل Renal vasculature وبالتالي بصير V.C ويقل ال renal blood flow , فيبعزز ال Renal
Ischemia

3يزود ال Inflammatory mediator Expression فبالتالي ييزود ال IL6 وال TNA وغيرهم من ال Mediator اللي بتعمل
Renal Cell Inflammation

4 بتقلل ال magnesium level ↓ ↓ ولما يقل ال mg عن معدله الطبيعي ييزيد ال Risk لل Nephrotoxicity

طيب مين المرضى اللي بيكون عندهم Risk Factor لل Cisplatin Toxicity
1 اللي عندهم بالاصل مشاكل بالكلى زي مرضى ال CKD

2اللي بيكونو ماشيين ع أدويه Nephrotoxic زي ال NSAIDs او ال ACEIs او ... Aminoglycoside

3استخدام جرعات عاليه من ال Cisplatin بتزود ال AKI risk

More than 50 percent of the drug is excreted in the urine in the first 24 hours following cisplatin
administration

Prevention of Cisplatin AKI

كيف بنعمل Prevention لل ... Cisplatin AKI

1 Administration of I.V saline

٩٩) بالعاده بينعطى المريض من 1-4 لتر خلال 24 hr

We prepare a solution consisting of 1000 mL of isotonic saline plus 20 mEq of potassium chloride and 2 grams of magnesium sulfate. We administer intravenously a minimum of 1000 mL of this solution over two to three hours prior to, and a minimum of 500 mL over the two hours following, the cisplatin administration. This fluid administration should be adequate to establish a urine flow of at least 100 mL/hour for twohours prior to, and two hours after, chemotherapy administration

لو المريض عنده ما يمنع ال Isotonic Saline

بنحاول نغير ال chemotherapy Regimen لغير ال Cisplatin
الا لو كان ال Cisplatin بيستخدم لل Cure او الحاله
Life threatening ..

Mannitol is frequently used to induce diuresis, although there is no evidence that this is required. It may be appropriate in select patients, such as those treated with high-dose cisplatin (≥ 100 mg/m²) ... and/or those with pre-existing hypertension
ل

و المريض Outpatient بنعمله Hydration

By 2-4 L + Mgsulfate (for 2-6 hour)

2) Avoid other Nephrotoxic Drug

3) use low and effective dose of cisplatin

Doses of cisplatin are generally not lowered in settings in which cure is the goal of therapy (eg, small cell lung and testicular germ cell tumors). germ cell tumors).

4) Use of cisplatin analogs — The less nephrotoxic analog carboplatin has been substituted for cisplatin in many chemotherapy regimens

5) ● Amifostine

ال Amifostine فيه Thiol group بتعادل ال Cisplatin Toxicity
لكن اغلب الدراسات بينت انه ال Amifostine بيقلل من ال Effect تبع ال Cisplatin
فيه بروتوكولات لساتها بتستخدم ال Amifostine ك Prevention
وفي بروتوكولات ما بتستخدمه
According To UpToDate

We do not use amifostine to prevent cisplatin-induced nephrotoxicity. The principal reasons include the availability of newer regimens that use lower doses of cisplatin or substitute carboplatin for cisplatin and the significant toxicity (nausea, vomiting, hypotension) and costs associated with the administration of amifostine. Furthermore, concerns persist about possible interference with the antitumor efficacy of cisplatin. Amifostine should not be used in settings in which chemotherapy can produce a significant survival advantage or chance of cure

□□□□□□□□□□□□□□□□

طبيب لو المريض صار معه AKI كيف رح نعمله Management

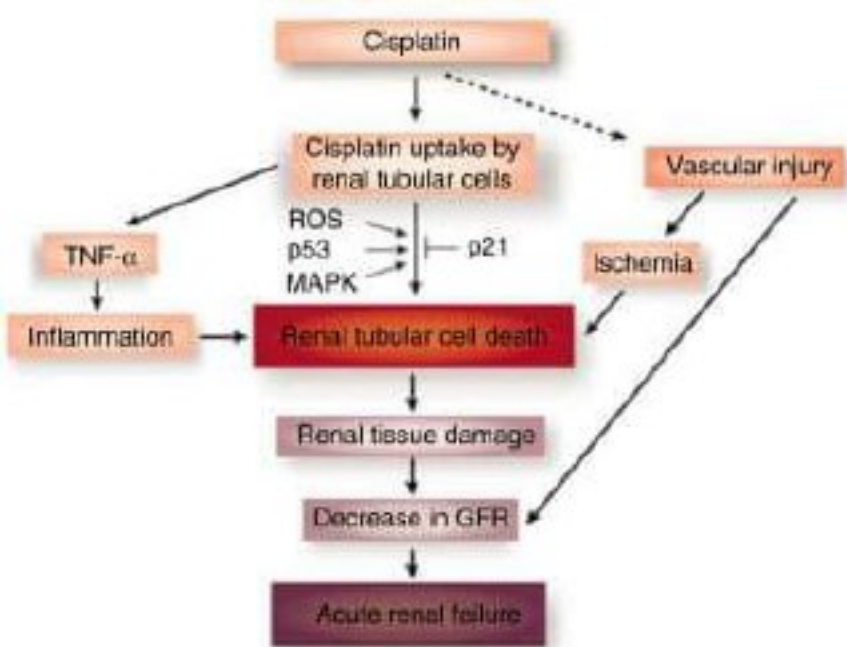
❖ اول شي بنعمل Discontinuation لل Cisplatin في الحالات اللي بتدخل ب .. Moderate- Sever AKI

If the inclusion of cisplatin in the treatment regimen is considered to be life-saving or life-extending, Hypomagnesemia ال بتصحح ال .retreatment with cisplatin may be considered after recovery from AKI

وعادة بنستخدم جرعات عاليه من المغنيسيوم

❖ لو صار عند المريض Salt wasting و volume depletion بينعطى I.V saline لحد ما يتزبط عنده ال Volume

#لعلي_أفيدك ❖



Female 44 years Old suffer From Rheumatoid arthritis she is on Corticosteroid Therapy

بتاخذ Prednisolone بجرعه 10 mg يوميا

فجأه دخلت بـ sever Fungal Infection ورح تمشي ع amphotericin B

بعد 4 ايام من ال amphotericin B لاحظنا ارتفاع ال SrCr وانخفاض بالبوتاسيوم والمغنيسيوم مع Distal Tubular Acidosis

يعني المريضه دخلت بـ AKI drug Induce ...؟

ال amphotericin B واحد من الادويه اللي بتعمل Reversible و Dose Dependent AKI

فبيبدا ال srcr يرتفع لما الجرعه تعدى 2-3 gm

وبيدخل المريض بـ Nephrotoxicity لو ال Cumulative dose عدت ال 4 gm ...

ال amphotericin B

طيب خلينا نشوف كيف ال amphotericin B بيأثر ع ال Kideny .

في عنا ميكانزمين من خلالهم ال amphotericin B بيعمل Nephrotoxicity

.. 1 vasoconstriction to renal Aretry

وبالتالي ببقل ال Renal blood flow وال .. GFR

2 Ditect Tubular Toxicity ..

الدوا بيرتبط بال cholesterol الموجود بال Renal cell membrane واللي بيعزز هاد الارتباط هو وجود solubilizing

agent بـ ال amphotericin B formulation اللي اسمه deoxycholate

ال amphotericin B

مين المرضى اللي بيكون عندهم Risk factor لل

amphotericin B Nephrotoxicity

1 Pateint taking Nephrotoxic drug

زي مثلا المريض ماشي ع Vancomycin او NSAIDs او غيرهم ...

2 Pateint with Kideny Disease

3 Dose of amphotericin B

The likelihood of renal disease is also dose dependent, with the risk of renal dysfunction being low

at doses of less than 0.5 mg/kg per day and a cumulative dose of less than 600 mg

ال amphotericin B

كيف ممكن نعمل Prevention من ال amphotericin B Nephrotoxicity

1 بنعطي المريض 1L من ال Normal Saline قبل ما ياخذ جرعه ال amphotericin B

2. بنعطي ال amphotericin B ب Slow Infusion

May be infused over 4 to 6 hours.

3. الافضل استخدام ال Liposomal amphotericin B بدل ال

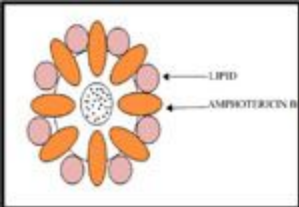
Conventional amphotericin B

- The liposomal preparation does not contain deoxycholate, which has direct tubular toxicity so less Binding to Tubular Cell

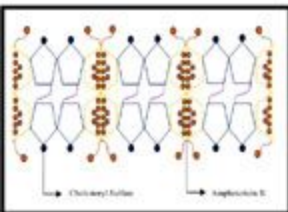
#لعلي_أفيدك

@Hadeel2333

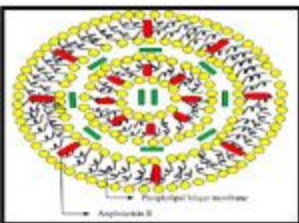




42-63% Nephrotoxic
Abelcet
 Lipid complex



25-40% Nephrotoxic
Amphotec
 Colloidal dispersion



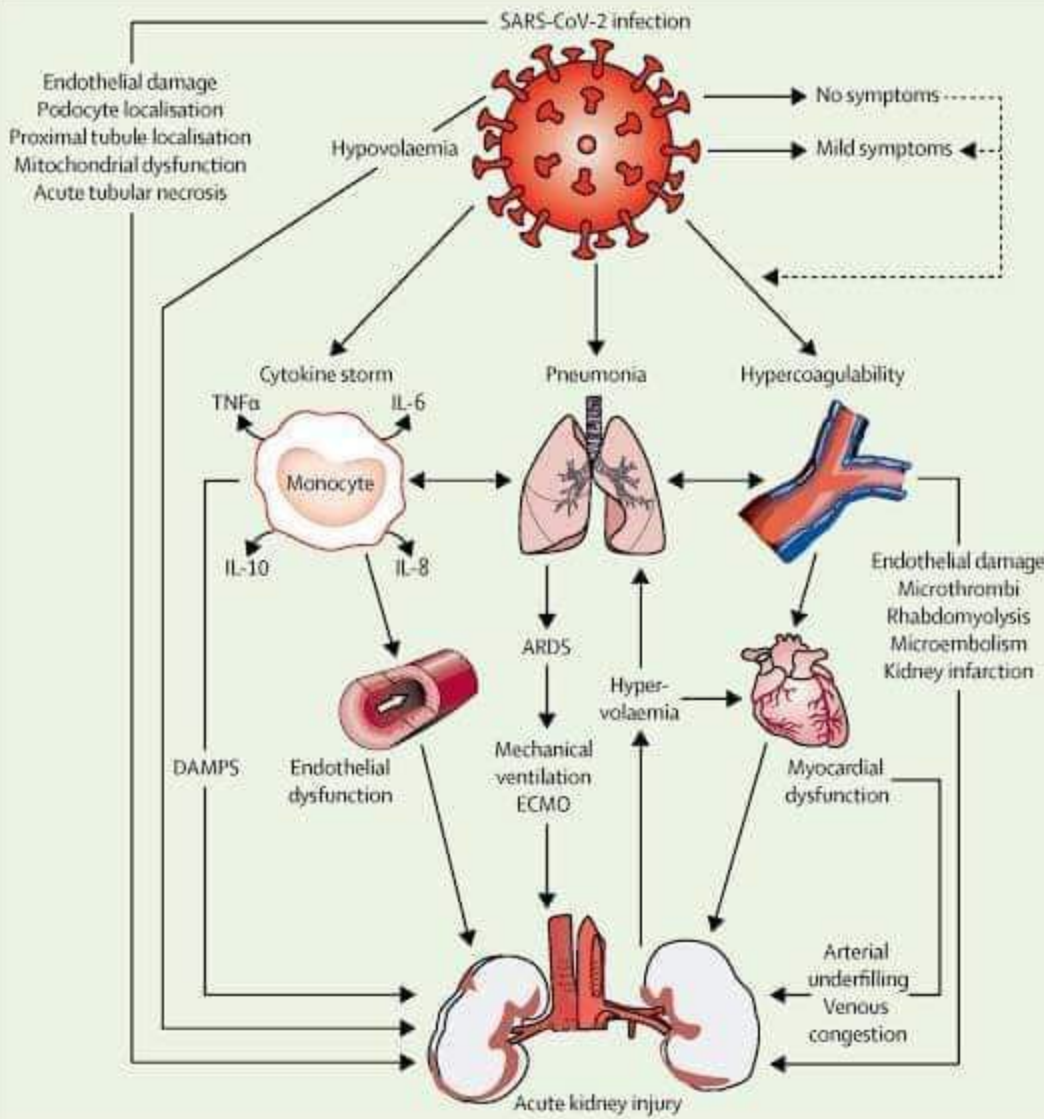
10-20% Nephrotoxic
Ambisome
 Liposomal

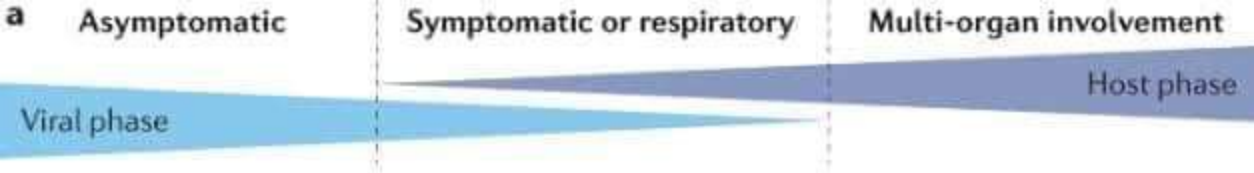
Amphotericin B
 (Low solubility,
 High molecular
 weight, Higher
 systemic
 toxicity)

Nanotechnology Approaches

- Liposomes (Reduced nephrotoxicity, high cost, poor stability)
- Nanoemulsion
- Nanoparticles
- Ultradeformable liposomes
- Dendrimers
- Carbon nanotubes
- Ethosomes
- Nanospheres
- Polymerosomes

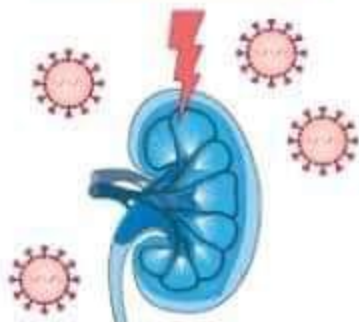
	TYPES	DOSE	IMPORTANT NOTE
	Conventional Amphotericin B	1-2mg/kg	DILUTION: Amphotericin B should always be diluted in dextrose.
	Liposomal Amphotericin B	3-4mg/kg	It should not be diluted in Normal saline [because amphotericin B gets precipitated in normal saline].
	Amphotericin B colloidal Dispersion [ABCD]	3-4mg/kg	PRECAUTIONS TO BE TAKEN: While diluting, Amphotericin B should be covered with foil or should not be exposed to sunlight.
	Amphotericin B Lipid Complex [ABLC]	5mg/kg	





b Mechanism for AKI

Direct viral effects



- Collapsing glomerulopathy
- Endothelial damage
- Coagulopathy
- Complement activation
- Inflammation

Indirect effects

- Fluid management
- Mechanical ventilation
- Nephrotoxins

Organ crosstalk

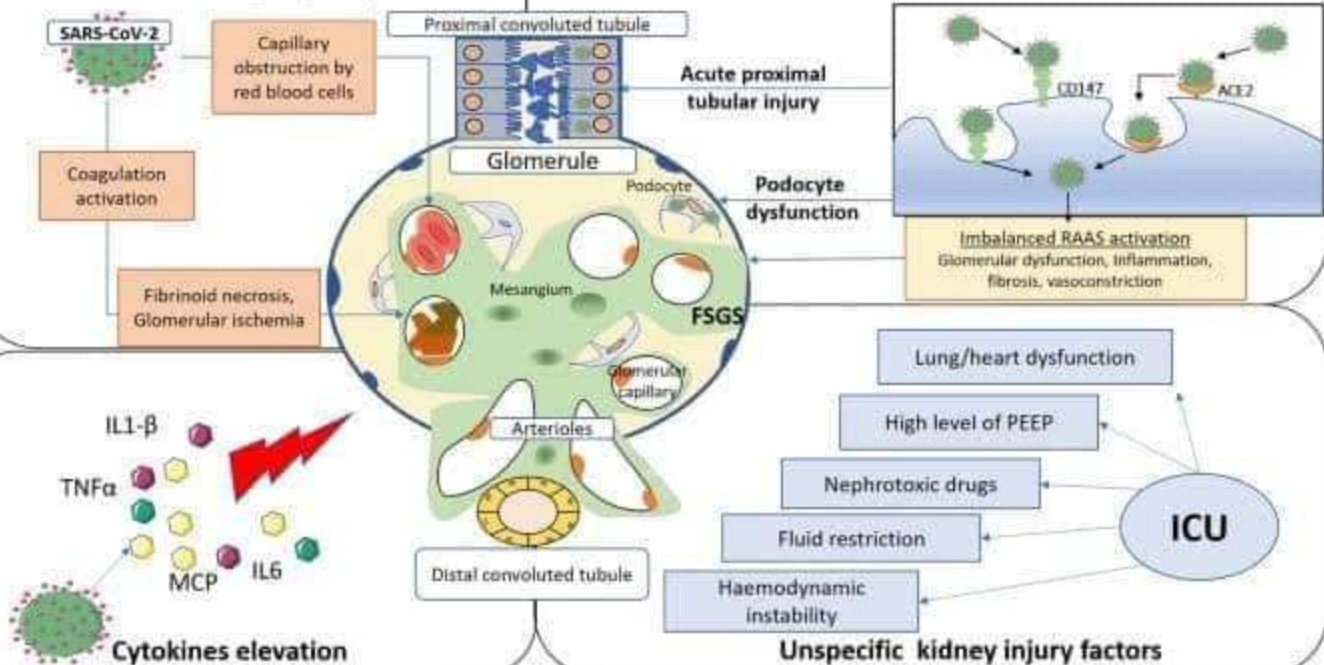
- Fever or sepsis
- Diarrhoea

- Hypovolaemia
- Acute tubular injury



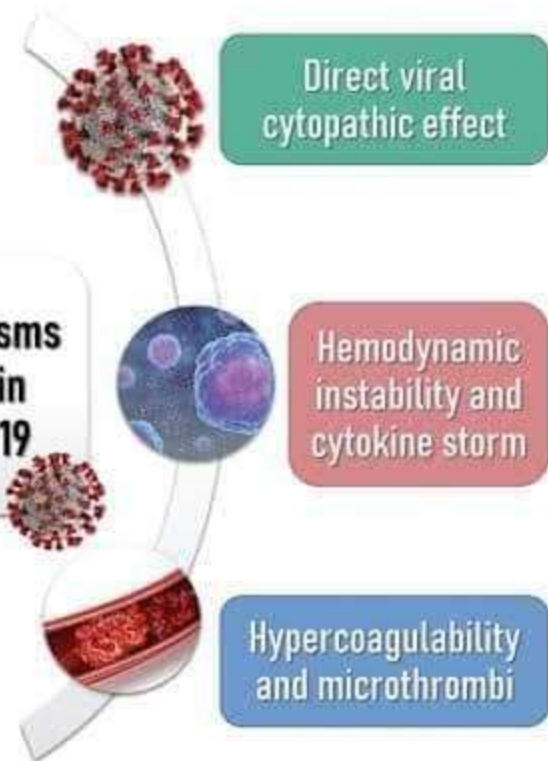
Vascular consequences of SARS-CoV-2 induced coagulopathy

Kidney invasion via SARS-CoV-2 entry in proximal tubular cells and podocytes





Mechanisms of AKI in COVID-19



- ❑ SARS-CoV-2 binds to ACE2 receptor, which is highly expressed in the kidney tubules and podocytes.
- ❑ SARS-CoV-2 was demonstrated in renal tubules in autopsy studies and isolated from urine sample of COVID-19 patients.
- ❑ Viral replication in podocytes could account for proteinuria reported in COVID-19 patients.

- ❑ AKI in ARDS patients could be part of kidney lung cross-talk.
- ❑ Many hemodynamic changes occur in ARDS patients.
- ❑ ATN was noted in autopsy study of COVID-19 patients.
- ❑ ATN is reported with volume depletion, cytokine storm, hypoxia, and shock.

- ❑ Innate immunity and coagulation pathways are linked.
- ❑ Cytokine storm can result in activation of coagulation factors and hypercoagulability.
- ❑ Recent clinical and autopsy reports reported an increase in DIC, small vessel thrombosis and pulmonary infarction.